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THE VALUE OF OPTIMISM IN MEDICINE.[1]

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I have been sorely puzzled in the selection of a topic for my address to you tonight. I preferred not to impose on a general Congress of Physicians and Surgeons a subject relating to my own specialty; I had not confidence enough in my powers, and too much consideration for you to attempt a more or less ambitious and comprehensive historical review of the advances, achievements, and possibilities of medical science, so that I finally decided simply to look back on the personal experiences of my own medical life and select from them some topic on which to say a few words to you.

As I look back on my medical life, the one thing that seems to stand out as having been most helpful to me, and which has enabled me more than anything else to accomplish whatever I have been able to do, seems to me to have been that I was ever possessed of a large fund of optimism; indeed, at times optimism was about the only resource I had left with which to face most unfavorable conditions and overcome serious obstacles; and it is, therefore, on the value of optimism in medicine that I want to speak to you tonight.

Optimism is a product of a man's heart rather than of his head; of his emotions rather than of his reason; and on that account is

[1] The president's address at the Eighth Congress of American Physicians and Surgeons, held in Washington, May 2, 1910.

rather frowned upon by many physicians whose scientific training naturally leads them to depend solely upon the qualities of the intellect, and look with suspicion upon any product of the emotions. We doctors are too apt to look upon "brains"—that is, a man's purely intellectual attainments—as the criterion of his chances for achievement in life, and to ignore and even deprecate those qualities which are closely related to his emotions as rather likely to mislead and hamper him in his career. And yet optimism is a prominent factor in anything a man may achieve in life. It is a mixture of faith and imagination, and from it springs the vision which leads him from the beaten paths, urges him to effort when obstacles block the way, and carries him finally to achievement, where pessimism can see only failure ahead. Optimism means energy, hardships, and achievement; pessimism, apathy, ease, and inaction. Optimism may and often does point to a road that is hard to travel, or to one that leads nowhere; but pessimism points to no road at all.

I have come in contact with many men of splendid attainments and opportunities who, by habit and education, have suppressed imagination and faith until their usefulness has been greatly impaired, and who accomplished little in life because the chill of pessimism ran in their blood, and the "qui bono" was the early deathblow to every impulse at accomplishment. Lack of faith and imagination has quenched achievement in many men whose intellectual attainments promised most fruitful careers.

It is, perhaps, true that the great majority of physicians, outwardly at least, appear to incline neither to pessimism nor optimism, and seem merely to float with the tide, without aspirations or ideals; but in reality few of them, in the innermost recesses of their ego, are entirely free from some degree of imagination and faith which they habitually quench, and which, if cultivated, would at least broaden the sphere of their activities and make life less colorless.

The doctor, whether he be a scientist and his life wholly given to scientific investigation in a laboratory, where reason and intellect reign supreme, or whether he be wholly a practising physician and surgeon in daily contact with suffering humanity in its struggle with disease, will need all the optimism he can cultivate if his life is to be as fruitful in results as it can be made. The scientist without optimism may be an admirable intellectual machine, who, it is true, is not likely to be led astray from the well-worn road of demonstrable and generally already demonstrated facts, and as such he will have his place in life; but he will never climb above the ruck, he will create and achieve little in the field of original research, unless faith in his own powers furnishes the incentive to constant effort and imagination leads him into an unexplored region to new methods and untried lines of investigation.

The professor of medicine and the laboratory director need

optimism if they are to inspire their students to do their best work, and they should beware how they quench, too often unfortunately with ridicule, the optimism of the young men who look to them for direction. Over-enthusiasm is not a very serious fault in a young man, and can easily be kept within bounds, and optimism in a student is a better incentive to work than pessimism.

The practising physician and surgeon must have optimism if he is to develop a full degree of efficiency in meeting the terrible emergencies of acute illnesses and accidents, or the long drawn out struggle with lingering and hopeless disease, and at the same time inspire his patients with a degree of optimism which means everything to them in the ordeals they have to pass through. To the practising physician and surgeon optimism is even more necessary than to the scientist, for besides moulding the doctor's character and guiding him in his decisions as to the case, his optimism is at once reflected to the patient and influences his condition accordingly. How great this influence may be we are learning more and more to appreciate. In his hour of need the patient has no means of judging of the physician's intellectual attainments; it is the faith that radiates from the doctor's personality that he seizes upon and that is helpful to him. Any encouragement that emanates from the physician will help keep up the patient's courage and carry him through long days of illness and suffering to recovery; and, where recovery is impossible, if the doctor's optimism—that is, his faith—is of the kind that extends to the future, not only here but hereafter, it may dispel for the patient much of the darkness and despair which brood over the end of life, and perhaps even illume for him that vast forever, otherwise so shrouded in impenetrable gloom.

Ian Maclaren's optimism was of this kind, and Dr. Grenfell's optimism is every day helping him to heal not only the sick bodies, but the broken spirits of men as well. This is the highest type of optimism the doctor may attain to, as its influence may reach not only to the physical, the intellectual, and the psychical, but even to that dim ethereal region of the spiritual, from which spring man's most sacred and cherished aspirations. This side of the doctor's life of service to humanity is known but to himself and to those who in the hour of death have turned to him for help; to the world this is a closed book, but what is written in its pages has helped to make the medical profession a benediction to mankind.

Perhaps the most brilliant and striking examples in our time of the value of optimism, each representing one of the two extremes of the medical profession—that is, experimental science and practical medicine and surgery—are Pasteur and Grenfell. I have chosen these two men as examples of optimism, each in his own sphere, because, widely different as have been their fields of labor, they each represent a type of optimism in medicine which, to a greater

or less degree, is the ideal of so many doctors' lives—the humanitarian type. The moving force in both Pasteur's and Grenfell's lives has been the relief of human suffering, and their intellectual attainments have been consecrated to this end. Personal ambition, the pride of intellect, or the love of fame has had little or no influence in urging them to their great achievements.

The man who, standing at the very threshold of the discovery of the germ origin of disease, did not hesitate to say, "It is within the power of man to cause all infectious diseases to disappear from the earth," must indeed have been an optimist. Pasteur's optimism led him unerringly to the solution of every experimental problem he started to solve, because his faith made him see nothing ahead but success, and his imagination led him to a solution of the most difficult problems when his reason alone would have failed. His hydrophobia work is a striking example of this. Who but an optimist would not have been discouraged at his repeated failures to find the specific microbe of hydrophobia which, in the light of all previous knowledge, was the first requisite to success in evolving a method of immunization? His faith saw in this no cause for discouragement, but only urged him to renewed effort, while his imagination led him to leave the usual methods, ignore the microbe, and search for the seat of the poison in the rabid animal; and when he had located this in the medulla, and not in the saliva alone, as hitherto believed, devise a method whereby the toxic medullas could be attenuated and transformed into a vaccine of graded virulence. But of what practical use would a vaccine be that had to be applied before the individual was bitten? No vaccine applied *after infection* had up to that time ever been found to be successful. That Pasteur was an optimist and had a vision is shown by his own words in April, 1884: "What I aspire to is treating a man after a bite with no fear of accident." And you all know that his vision became a reality, and that practically the conquest of this most dread disease is an accomplished fact.

The moving force in the great medical humanitarian achievements of Dr. Grenfell is the highest type of optimism; a faith which includes not only that which is seen and temporal, but the unseen and eternal as well; and on this, which to the pessimist would seem an uncertain and emotional basis, he has built up a work which has arrested the attention and won the admiration of the civilized world. That kind of optimism which extends to the hereafter is in Dr. Grenfell no mere idealist's vision, but a very real force to be reckoned with in this world if it enables a man in so few years to accomplish what he had done. It has enabled him in the face of constant and imminent dangers by land and by sea to bring skilled medical and surgical treatment to a suffering and helpless community; single handed, without modern aids and appliances, to perform delicate and difficult surgical operations under most

unfavorable conditions; to throttle entrenched vice in its stronghold and cast it out; to turn aggregations of squalid huts and drunken, poverty stricken, and despairing people into thriving, well-ordered, and productive communities. Had Dr. Grenfell lacked an inexhaustible fund of optimism, had that faith in God and man, which to him is the most present reality in life, not been his, had be believed only in "that which could be reduced to a formula," had the "knowable" been for him the "only real," in spite of his intellectual attainments the world would have lost the inspiration of his matchless career, and the inhabitants of the Labrador coast would have remained plunged in the gloom of degradation, despair, and misery.

It is to this high type of optimism that we owe, through the untiring labors of Richard Cabot, the social service department of the tuberculosis dispensary. The success of Dr. Cabot's work has been due primarily to his own personality, which so strongly reflects his faith and his ideals, and which has inspired those whose efforts he directs. This new departure in medical work is not scientific in its character, but Christian and humanitarian. It is being taken up as a regular part of every modern dispensary and hospital, and extended to relief measures among children, chronic invalids, and convalescents, and promises in time to revolutionize the whole character of hospital and dispensary methods. The degree of its success will always greatly depend, however, on the personal faith and enthusiasm of the physician as communicated to those who work under his direction. The far-reaching possibilities of this new departure in humanitarian medicine may be gathered from the following sentence taken from a recent address of Dr. Milton J. Rosenau: "The object of preventive medicine is, perhaps, not so much to save as to prolong life, and there is no use in prolonging life unless we can make healthier, better, cleaner, happier lives."

If there is no room for pessimism in the doctor's individual career there is no room for pessimism in our profession, for its ideals and the goal toward which it is moving so rapidly are pregnant with optimism. The conquest of disease by prevention, though disease is the source of the doctor's livelihood, the placing ever at the disposal of the poor, without money and without price, the greatest gifts of learning and skill at our command, the strangling of deception and quackery in our midst by education of the people, are standards which can only be inaugurated and upheld by the highest type of optimism.

Optimism is the one thing that is within the reach of us all, no matter how meagre our intellectual equipment, how unpromising our outlook at the start, or how obscure and limited our careers may be. It was about my only asset when I built my first little sanitarium cottage on a remote hillside in an uninhabited and

inaccessible region. Viewed from the pessimist's standpoint, that little cottage as an instrument of any importance in the warfare against tuberculosis must have appeared as a most absurd and monumental folly. Optimism made me indifferent to neglect and opposition and blind to obstacles of all kinds during the long years of struggle before the value of sanitarium treatment became generally recognized. It enabled me to undertake the culture of the tubercle bacillus and delve in the complex problems of infection and artificial immunization, though I had no knowledge whatwhatever of bacteriology, no laboratory, no apparatus or books. It has steadily upheld my faith in the possibility of ultimately attaining to an immunizing treatment for tuberculosis in spite of many discouragements and years of fruitless work.

Optimism enabled me to assume for over a quarter of a century the financial support of my work, and though the little cottage grew to be a village, and the workroom in my house became a well-equipped laboratory, though their support each year required large and increasing sums these have ever been forthcoming.

In a long life which has been lived daily in contact with patients beyond the reach of human skill, who through months and even years of hopeless illness looked to me for help, I have indeed had need of all the optimism I could cling to. It has ever been a precious asset to me, and I hope to those about me as well, and has never entirely failed me.

Let us not, therefore, quench the faith nor turn from the vision which, whether we own it or not, we carry, as Stevenson's lantern bearers their lanterns, hidden from the outer world, and, thus inspired, many will reach the goal; and if for most of us our achievements inevitably must fall short of our ideals, if when age and infirmity overtake us "we come not within sight of the castle of our dreams," nevertheless all will be well with us; for, as Stevenson tells us rightly, "to travel *hopefully* is better than to arrive, and the true success is in labor."

THE TREATMENT OF ARTERIAL HYPERTENSION.

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Although encountered in a variety of diseased conditions not primarily vascular in character, high blood pressure is most frequent in association with arteriosclerosis and chronic nephritis. It plays a leading role in the clinical history of these two diseases, especially the latter, and furnishes so preponderant a share of the

subjective discomforts as frequently to constitute an urgent indication for treatment. The inveteracy of this development bears a much more intimate connection with the element of toxemia than with the degree of arterial degeneration. Were this not the case we would expect to encounter the highest pressure readings in senile calcification of the arteries. For the same reason we might anticipate higher pressure values in arteriosclerosis than in chronic nephritis, because of the more essentially vascular character of the former disease. This is against the rule in both instances. In chronic nephritis we meet with the highest pressures observed and the more toxic the case the more pronounced and inveterate is the element of hypertension. Uremia furnishes the most extreme excursions above the normal. In cases in which the inroads of disease have rendered the kidneys unable to depurate the system, and when collateral channels cannot be sufficiently invoked to offset the renal deficit it will be found impossible by any means at our command materially to influence the resulting hypertension. In actual practice it will be found that the cases displaying the most irregular blood-pressure are those in which the toxic factor prevails. What the pressor toxins are we have as yet no clear view, but the general contention is that they consist of certain abnormal bio-chemical products. Clinical experience furnishes us with many suggestive hints pointing to the intestinal tract as one at least of the sources from which pressor toxins originate.

In arterial hypertension the heart is the organ that bears the brunt of the circulatory disturbance. In the early stages of hypertension the muscular part of the arterial wall hypertrophies in response to extra work (hypermyotrophy). At this stage the vessel is still elastic, though thickened and hypertonic, and nitrites will successfully lower blood pressure. As the process advances degenerative changes more and more destroy the muscular tissue and vasomotor response progressively diminishes until the nitrites may totally fail to lower blood pressure. Peripheral resistance increases in this manner with the stage of the disease. At first under the influence of the same causes as affect the arteries, and with the added burden of furnishing to the tissues an adequate fluid interchange, the myocardium thickens just as does the myarterium. Both the heart and arteries hypertrophy together. Finally as the disease advances the limit of the heart to increase further its functional area is reached, the cardiac and arterial hypertrophy no longer run parallel, but enter into conflict (Ewart). The arteries continue to thicken and stiffen, the heart wall to thin. The stage of heart failure has begun. The sequence of events occurring in the heart are first hypertrophy and finally dilatation in the face of continued overstrain. The clinical events at this stage are those which characterize progressive heart failure. The secondaries and complications of prolonged hypertension will be determined by the relative ability of the various organs to endure

the excessive strain. On the part of the heart we observe hyposystole and asystole, of the kidneys albuminuria and uremia, of the arteries atheroma. A cerebral vessel may give way and apoplexy close the scene. How long the final breakdown may be postponed will depend on the inherent vitality of the vascular tissues and the care and circumspection with which the patient treads his way amongst the pitfalls that beset his path.

The treatment of arterial hypertension constitutes a problem of much interest. High blood pressure being essentially no more than a vascular reaction against the presence of toxins in the circulating blood, the primary indication is detoxication. To accomplish this purpose we are forced to depend on the regulation of the diet and general hygiene and stimulation of the various emunctories.

The dietetic control of hypertension is too often interpreted as a simple restriction of flesh food. Excess of meat proteins unquestionably is harmful in this condition and on principle the diet should embody a strict regulation in this particular. We should, however, not rest with simple qualitative measures of this kind. Individualization is as necessary and important in this matter as in the application of any other therapy. The stage of the disease and the physical type of patient must be given due weight. To enforce a non-nitrogenous dietary does not exhaust the indications in any large percentage of cases. To place a strict embargo against meats and then permit a patient with high tension unlimited indulgence in other varieties of food is to invite failure. Even in health such a procedure with the average adult leads to excessive intake, lack of satisfaction, increase in weight with impairment of vigor. Digestive plethora whether of carbonaceous or protein food elements is harmful. Less toxemia will result and certainly less work be required of the organism to appropriate its quota of nitrogen from flesh than from vegetable proteins. A certain concession in the direction of meats may be allowed, especially in non-nephritic cases, the midday meal being chosen for the meat ration and its quantity limited within physiological bounds. The activities of the individual may to an extent govern the quantity permitted. Quantitative limitation should to a large extent take the place of qualitative restriction, moderation in all directions being enjoined. High pressure cases largely conform to the corpulent sedentary type and an all-round reduction in food intake is indicated. The proper diet in such cases will result in a reduction in weight coincidently with a reduction in pressure. For clinical purposes it is necessary to take note of that group of hypertension patients who eat moderately, but whose intestinal processes are faulty and who consequently may become toxemic on relatively spare rations. It is necessary here to gauge carefully the digestive capacity and let this factor rather than theoretical qualitative considerations dictate the food list. The weighing scales may very wisely be consulted to point the result of our dietary control.

Corpulent individuals should lose gradually in weight, spare nervous patients should at least not be reduced, but rather should gain somewhat in weight. Above all we should not tamper with the diet to so great an extent as to undermine the strength of our patients, nor by too great particularity in our restrictions engender morbid tendencies toward food.

The most harmful combination in plethoric cases of hypertension is constituted by the indulgence of the appetite, which is usually excellent, and physical indolence. This is shown in practical clinical observation by the Monday morning rise in blood pressure resulting from the inactivity of Sunday with the increased intake of a more luxurious fare on that day. An excess of twenty points or more above the usual average is often noted on Monday morning. Flatulency is a prominent symptom and hypertensive crises frequently coincide with tympany and belching. Bilious symptoms often initiate cardiac distress, palpitation, and angina. The diet should as far as possible be directed to control the intestinal fermentation. An all-round quantitative reduction of food intake will be found to accomplish this much better than qualitative measures alone. At any time during the course of a case we may be called upon to meet the emergency of an acute increase above the usual average pressure reading. Very suddenly and often without apparent explanation 40 or 50 mm. may be added to a pressure already abnormally high. At such times the heart may falter and apoplexy prodromes appear. In nephritic cases these sudden increments are usually uremic in origin. During such hypertensive crises a period of starvation and restriction of fluids may become advisable, or we may with advantage follow the suggestion of Haig and enforce for the term of such increase a diet consisting solely of bread and fruit.

The foregoing dietetic considerations apply to sthenic cases during the period of cardiac stability. When dilatation has supervened and symptoms of cardiac incompetency become pronounced increasing difficulty will be encountered in furnishing a diet suitable to the control of toxemia and digestive discomfort. The procedure must follow the indications of expediency and the problem be solved on an individual basis along the lines which govern the hygiene of cardiac invalids generally. The advent of secondary low blood pressure with its invariable vicious abdominal circle will mark the failure of all dietetic endeavor, assimilation being so badly impaired as to defeat all efforts aimed at digestive control.

At the outset the patient should be taught to avoid the use of salt on the food after it is cooked. This is a measure of possible utility in controlling tension and by inaugurating the practice early in the case the patient is prepared for the later stages of his malady when salt restriction becomes imperative. Restriction of fluid intake is a matter of small importance during the stage of cardiac competency. Even the generous imbibition of water during this phase of the case

does not suffice materially to raise the blood pressure and a distinct advantage to elimination is gained by abundance of fluids. Later on when the heart begins to fail it is but common sense to restrict within moderate limits the fluid intake.

Not only should the diet be made the subject of exact instruction to the patient, but also every detail of importance in the personal hygiene: the exercise, hours of work, care of the bowels, clothing, baths, etc. A grave mistake is made if we interfere too greatly with these patient's activity. The hours of work should be regulated within moderate bounds so as to avoid overstrain and reduce within safe limits nervous wear and tear. Exercise in the open air is absolutely essential. Overstrain, sudden exertion, and over-fatigue being unquestionably harmful are to be emphatically interdicted. Although the primary effect of exertion is to elevate the systolic reading, this increase is transient and is followed by a subsidence of pressure to the original level or even an eventual slight diminution. Cardiac fatigue lowers blood pressure and quickens the pulse. Sudden severe exertion and excessive fatigue are fraught with danger. Walking, golf, sailing and rowing constitute the best forms of exercise for these subjects. When circumstances permit the patient should seek climatic conditions which will permit of such moderate out-of-door activities during the different seasons.

Many kinds of baths have been advocated for the reduction of blood pressure. The procedure usually employed consists of heat to produce diaphoresis, either by means of the electric light or hot air cabinet followed by Scotch douche, Scotch rub, friction, etc. The immediate effect of these measures is to produce a drop of from ten to twenty points in the systolic reading. This reduction proves very transient in the majority of instances, the blood pressure quickly returning to the former level. The blood pressure chart may not appear to be greatly influenced by hydrotherapeutic measures and yet it will frequently be found that the symptoms seem much improved by the treatment. The same thing is true of simple sweat baths. The routine employment of sweating twice or thrice weekly is often found of decided benefit. Although they may not materially lower the blood pressure they apparently aid in preventing the sudden increments which result in discomfort and danger to the patient.

Perhaps the best single measure in the hygiene of hypertension is the morning purge. "Dickinson's morning purge" has had a recognized vogue for many years in granular kidney. Each morning before breakfast a sufficient dose of some saline laxative or aperient water should be administered. It serves the double purpose of elimination and depletion. I confess to a preference for Glauber's salt in these cases. Two or three free watery evacuations daily should be secured. In addition to this measure blue mass or calomel may with advantage be given once every week or ten days as a detoxicant.

A point at present in dispute is the propriety of employing vasodilator drugs for the regulation of high blood pressure. Under the authority of Krehl and Janeway the view has been advanced that high blood pressure is a compensatory process. Janeway says "whatever the exact method of its production we cannot avoid the conclusion that the hypertension expresses an attempt of the organism to maintain an adequate speed of capillary flow through the kidney or other organ which would be impossible without it."

As a result of the promulgation of such views drug control of hypertension has come to be regarded in many quarters as a tampering with nature, hence unscientific. This ultraconservative stand has undoubtedly served a good purpose by restraining somewhat the ardor of those who would have carried on too vigorous a campaign against this symptom. Attractive as this theory appears, and perhaps applicable to cases of contracted kidney, it fails to satisfy when applied to that large class of cases in which no renal disease exists and yet excessive pressure values obtain. As a matter of fact, there is no certain correspondence between the amount of urine excreted and the degree of blood pressure. This is true in health and also in hypertension cases.[1] The administration of a nitrite to lower blood pressure will as often be attended by an increase as by a fall in the amount of urine (Leech). Hare takes his stand against drug regulation of high pressure on the ground that the tissues have become accustomed to a new standard of pressure with which it is unwarrantable to interfere. There is undoubtedly much truth in what he says and the wise physician will not meddle too much with the *status quo*. If he is not guided by a wise conservatism in the administration of vasodilators, the physician may be chagrined to find his patient more disturbed and vastly more uncomfortable with the pressure lowered than he was before. This is, however, no fault of the drug, but of the way it was employed. Properly exhibited I believe that a certain measure of vascular drug therapy is applicable to these cases and with the greatest benefit.

It goes without saying that in so far as high pressure is dependent an anatomical changes in the vessel walls no influence can be exerted by drugs. If we administer $\frac{1}{100}$ grain of nitroglycerin to a patient with a pressure of 200 mm., we will often obtain a drop of 20 to 30 points. It is obvious that the high pressure in this patient is not wholly due to anatomical changes, but that there is as well a certain spastic condition of the vessels which has been relaxed by the nitrite. This corresponds to the hypertonus of Russel and represents at the moment the irritative effects of circulating toxins. It is this spastic contraction of the vessels that causes much of the functional distress of these sufferers and is to blame for the irregularities of the blood pressure chart.

[1] Jour. Amer. Med. Assoc., April 13, 1907, p. 1247.

It may well become the object of treatment for it apparently serves no good purpose to the organism, but on the contrary endangers the integrity of the vessels and subjects the heart to overstrain. In the nitrites and iodides we possess the means of relieving to some extent this vicious element. I am far from advocating the use of vaso-dilators in all cases.

When the pressure lies within moderate bounds and there are no subjective symptoms nor physical signs of disquieting character, no active interference with drugs is necessary. The higher above 200 mm. the pressure rises the nearer impends the inevitable breakdown of heart or artery, and we should proceed to estimate what advantage we may secure by vasodilator medication. We have two important points to determine as a preliminary before initiating a course of vascular drug therapy. One of these is the degree to which vasomotor response is retained by the arteries and the other is the functional adequacy of the heart muscle. Following the suggestion of Oliver, we may secure a rough estimate of the arterial response by administering $\frac{1}{100}$ grain of nitroglycerin and carefully noting its effect on systolic pressure for at least one half hour. The reduction secured by the nitroglycerin will afford a rough index of what may finally be accomplished by routine vascular medication. Should no response or but a trifling one attend the action of the nitro-glycerin, it will generally speaking prove a futile undertaking to inaugurate vasodilator treatment. This preliminary trial with nitro-glycerin should be undertaken with some caution in patients who have not previously experienced its action. It is better to give it in several fractional doses at short intervals instead of in one dose. If this precaution is not observed patients may now and then develop syncope or severe circulatory depression. This happened to me recently, when an elderly lady to whom $\frac{1}{100}$ grain of nitro-glycerin was administered developed every evidence of shock, lost consciousness, and did not recover vascular tone for one-half hour.

If the blood-pressure range is excessive and especially if observations indicate the presence of vascular spasm nitrites may be begun. The nitrite best suited for routine use is sodium nitrite. Its action is sufficiently prolonged to qualify it for this purpose and its administration is not attended by the disagreeable cerebral discomforts that frequently follow more active vaso-dilators (nitroglycerin, erythrol-tetranitrate). It may be begun in doses ranging from one-half to three grains at intervals of from two to six hours depending on the severity of symptoms. It should be invariably begun in the smallest dosage and gradually increased until the effect desired is produced, or its failure demonstrated. Its therapeutic action can often be observed in the blood pressure chart, but not always. A certain proportion of cases show a reduction of from 10 to 15 per cent. in the average blood pressure range and along with this reduction experience a sensible relief of symptoms. Not infrequently the blood pressure

chart may show no reduction and even at times a slight rise in average pressures. We are not to conclude from this that the drug is inoperative, for such patients occasionally will testify that their cardiac irritability, dyspnœa, or cerebral discomforts have undergone a distinct amelioration. Such individuals may be considered favorable subjects for nitrite therapy. A certain proportion of patients are distinctly worse under nitrite therapy. This is almost always the case in the hypertension of Bright's disease. Nitrites often cause a marked fluctuation without reduction in the average pressures, but with the effect of markedly aggravating cardiac and cerebral distress. Such cases are unsuitable for vaso-dilator medication. As a general rule nitrites should not be employed in Bright's disease except to meet emergencies.

For routine use in favorable cases the following combination, originally suggested by Brunton, will be found excellent: Sodium nitrite, 2 to 3 grains; potassium nitrate, 10 grains; potassium bicarbonate, 10 grains. To be taken in hot water three times a day after meals. Spiritus ætheris nitrosi in teaspoonful doses, several times daily, will often be found sufficient to modify the discomforts of high pressure.

The employment of the iodides coincidently with nitrite medication will at times be found to improve arterial response. In cases characterized by advanced arterial degeneration and impaired vasomotor tone iodides are indicated rather than nitrites and should be given in a routine manner for long periods.

The fact that the case is one of hypertension does not necessarily imply that we must confine our efforts to the relief of the vascular condition. It is often quite as essential to support the heart. We are frequently appraised of the existence of ventricular inadequacy, especially in long-standing cases of hypertension, by the existence of œdema, gallop rhythm, or the occurrence of attacks of acute dyspnœa. With or without such indications to guide us it will often become advisible to resort to some method for the estimation of the heart reserve. A rough and ready clinical means for estimating the functional power of the heart is Graüpner's test. This test rests upon the fact that the work reaction of weakened hearts after a measured amount of exertion differs from that of normal hearts. Graüpner used a weight and pulley ergometer. A measured amount of stair climbing may be made to answer equally well. The number of foot pounds of work is reckoned by multiplying the body weight in pounds by the number of stairsteps climbed. Graüpner describes the reaction in normal hearts (normal Erholung) as follows: after the pulse rate has risen as the result of exertion and again fallen to normal which happens quickly in healthy subjects, the systolic blood pressure begins to rise reaching its maximum some minutes later than the pulse rate, gradually falling thereafter to or sometimes below the original level. In weakened hearts if the damage is but

slight the reaction of the blood pressure still occurs, but is delayed and perhaps diminished in degree. In seriously weakened hearts there may be no reaction whatever, the blood pressure declining from the start, then gradually reascending to the usual level. According to my experience the usual reaction, on the part of the blood pressure is an immediate rise of from 20 to 40 mm., coincident with the increase in pulse rate. Almost at once the pressure begins to fall again and in from ten to twenty minutes has reached its former level. In seriously weakened hearts this primary rise of pressure is but slight, usually a few degrees only, and is almost immediately followed by a decline which progresses until the pressure may register

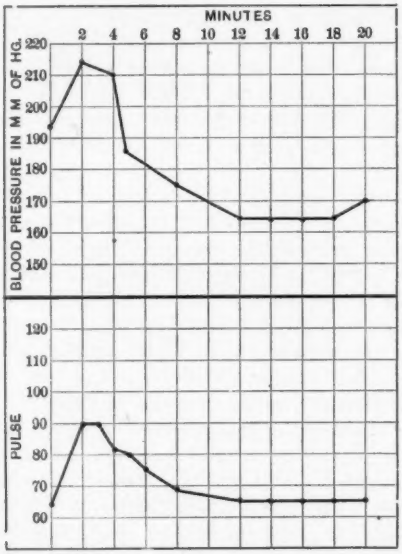
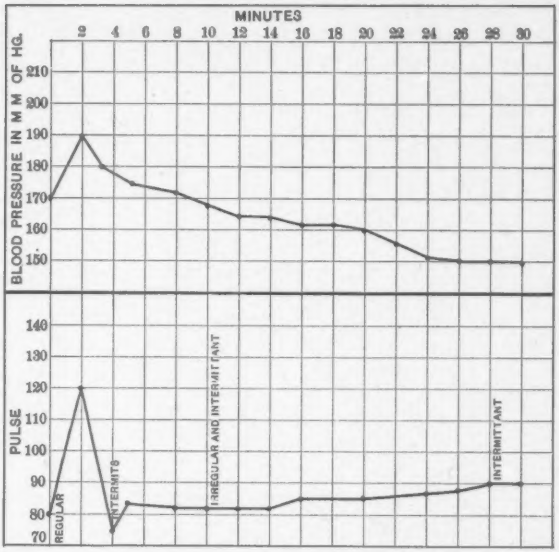


FIG. 1.—C. B., aged sixty years. Heart much enlarged; systolic mitral murmur; weak ventricle. Work = 8600 foot-pounds in three minutes.

30 mm. or more below the original point (Figs. 1, 2 and 3), the pulse increasing in frequency and perhaps becoming unsteady as the blood pressure falls. This type of reaction may be interpreted as showing the ventricle first reacting but proving unequal to the task of maintaining pressure with a compensatory increase in pulse rate.

Although Graüpner's method is of unquestionable value in assisting us to a better demonstration of muscular insufficiency my experience would lead me to interpret the findings secured thereby, in a liberal rather than a literal manner. A negative finding has not the same value as a positive one. Quite recently I elicited a pretty satisfactory reaction from an old gentleman with hypertension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2 4 6 8 10 12 14 16 18 20 22 24 26 28 30
BLOOD PRESSURE IN M M OF HG.
210 200 190 180 170 160 150
PULSE
140 130 120 110 100 90 80 70
REGULAR
INTERMITT
IRREGULAR AND INTERMITTANT
INTERMITTANT

FIG. 2.—G. H., aged sixty-nine years. Myocarditis with a weak ventricle. Work = 9600 foot-pounds in three minutes.

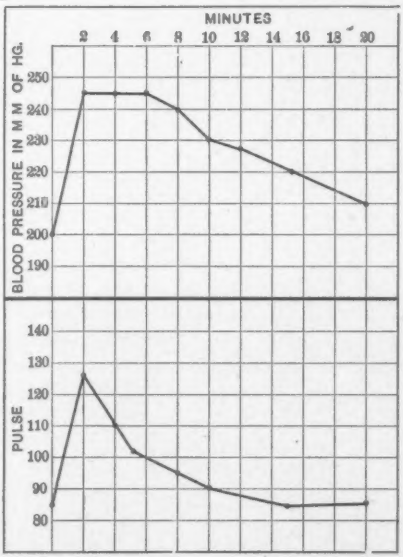

FIG. 3.—Mrs. W. K., aged seventy-eight years. Osteriosclerosis; myocarditis; relative mitral leak. Work = 2500 foot-pounds in three minutes.

yet notwithstanding he died within a fortnight of asystole (Fig. 4). The greatest caution should be exercised in the administration of nitrites in cases displaying indications of ventricular weakness. The effect of nitrite therapy in this type of case is often to produce rapid heart action, depression, and dyspnœa. If administered at all nitrites should be given very guardedly in conjunction with cardiac tonics.

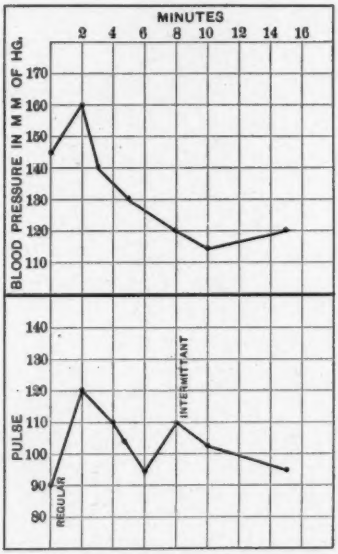

FIG. 4.—S. F., aged seventy-six years. Hypertension; heart greatly enlarged; mitral murmur. Work = 15,000 foot-pounds in four minutes.

When the indications point to cardiac insufficiency the greatest emphasis should be placed on the dangers of over-exertion, and cardiac tonics may be cautiously introduced. Because the case is a high pressure one need not deter one from using digitalis, as it is rare that in physiological doses this drug increases pressure sufficiently to endanger the vessel wall. On the contrary, it is not rare to note a fall in blood pressure under digitalis, probably because the drug by improving pulmonary circulation procures better oxygenation of the blood.

THE HEMORRHAGIC DISEASE OF THE NEWBORN, WITH SPECIAL REFERENCE TO BLOOD COAGULATION AND SERUM TREATMENT.

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The object of the present communication is to draw attention to the little recognized, clinically important fact of delayed or lost coagulation in the hemorrhagic disease of the newborn, and to discuss this in the light of recent investigations on the physiology and pathology of blood clotting. Two cases will first be briefly described.

Case I.—*Multiple hemorrhages; total failure of blood coagulation; transfusion.* D. G., male, eleven days old. Mother's history: Fourth pregnancy; first two resulted in miscarriages, one at four months, one at two months, third child is alive and well. Mother has just been operated upon for abscess of the breast. There are no bleeders in the family. The father denies syphilis. Child was born at full term; normal delivery; breast fed; well until the seventh day, when it began to vomit after feeding. The vomitus was black. On the eighth and ninth day this vomiting continued and the stools were loose and bloody. For the past two days there has been bleeding from the nose and mouth.

Physical examination, September 11, 1908. General condition fair. Bleeding from the mouth. Skin moderately icteric. Ecchymosis over the lumbar spine. Spleen palpable one finger's breadth below the free border of the ribs. The liver not enlarged. Slight enlargement of all the lymph nodes. Temperature, 99° F.

September 12. The child was admitted to Dr. Koplik's service in Mount Sinai Hospital. At 4 P.M. an injection of 10 c.c. of horse serum was given and the coagulation time of the blood was estimated. In taking the coagulation time a modification of Milian's method was used. A drop of blood 5 mm. in diameter was taken on a cover slip from a prick in the finger. The slip was inverted on a hollow ground slide and ringed with albolene to prevent evaporation and exclude air currents.[1] With this method the moment of coagulation can be accurately determined by the failure of the drop to sag when the slide is tilted.[2] Drops of the child's blood taken in this way were kept for four days and showed no sign of coagulation. Experiments done with the blood at this time will be described below.

[1] The tests were done at room temperature. In the cases here described this was accurate enough. But when careful comparative measurements of coagulation time are necessary a constant temperature is, of course, extremely important. See Addis, Quarterly Journal of Experimental Physiology, 1908, vol. i, No. 4.

[2] Hinman and Sladen, Johns Hopkins Med. Bulletin, 1907.

The injection of serum had no effect either on the coagulation time or the hemorrhages. The child's condition became worse and a transfusion was determined upon. The father, for reasons which need not be considered here, was chosen as the donor.

Four or five hours before the transfusion, which was performed by Dr. A. A. Berg, the blood examination showed: Red blood cells, 2,800,000; hemoglobin, 45 per cent.; white blood cells, 27,600; polynuclear cells, 41 per cent.; mononuclear cells, 59 per cent.

Bleeding from the mouth continued up to the time of the transfusion, when the hemoglobin was 30 per cent. As the child received blood the hemorrhage immediately stopped. During the course of twelve minutes the hemoglobin rose from 30 per cent. to 90 per cent. and the child, which at first had been of a waxy pallor, became red and then extremely cyanotic. The transfusion was then discontinued. Blood obtained from the child just before the transfusion failed to clot at all. At the end of the transfusion the child's coagulation time was the same as that of the father's—three and one-half minutes.

September 13. Twelve hours after the transfusion the general condition was very good; temperature, 99°; no bleeding; stools still tarry, probably due to admixture of blood from the previous day. Blood examination: Hemoglobin, 99 per cent.; red blood cells, 7,860,000; white blood cells, 24,200; polynuclear, 46 per cent.; mononuclear, 54 per cent.; coagulation time, three and three-quarters minutes.

September 14. The condition was unchanged. There was no fever, and no hemorrhages. The stools did not contain any blood. Blood examination: Hemoglobin, 95 per cent.; red blood cells, 5,660,000; white blood cells, 10,000; polynuclear neutrophile, 50 per cent.; polynuclear eosinophile, 2 per cent.; polynuclear basophile, 1 per cent.; mononuclear, 47 per cent.

September 15. Temperature was 101°. There was a purulent discharge from the left ear, but no hemorrhages. Blood examination: Hemoglobin, 110 per cent.; red blood cells, 6,350,000; polynuclear neutrophile, 55 per cent.; polynuclear eosinophile, 1 per cent.; mononuclear, 44 per cent.; coagulation time, seven minutes.

The urine was collected and measured for forty-eight hours following the transfusion.

Date.	Diet.	Volume.	Sp. gr.	Total nitrogen.	Ammonia nitrogen.	Uric acid nitrogen.
Sept. 14	Breast milk, 10 oz. Water, 1 oz. (330 c.c.)	54 c.c. 16.5% of intake	1012	0.7	0.07 10% of T. N.	0.173 24.2% of T. N.
Sept. 15	Breast milk, 7½ oz. Water, 8 oz. (450 c.c.)	175 c.c. 38.8% of intake	1001	0.42	.....	0.107 25.5% of T. N.

There was considerable serum albumin in the urine. Sugar reaction was negative. Microscopic examination showed ammonium urate and a few uric acid crystals. The quantity was somewhat diminished as compared with figures given by Shiff,[3] Camerer,[4] and Reussing,[5] who state that 62 to 68 per cent. of the fluid intake is excreted as urine in an infant of this age. The nitrogen in the urine computed after removing the albumin was 0.7 and 0.42 grams respectively. The nitrogen in the food for the second day was 0.4 grams, showing very probably no increased excretion during the first day and an even balance on the second day. The ammonia nitrogen was 10 per cent. of the total nitrogen. The uric acid was both quantitatively and relatively increased. On the first day there was an excretion of 0.173 grams of uric acid, being 24.2 per cent. of the total nitrogen in the urine. On the second day the excretion of uric acid nitrogen was 0.107 grams nitrogen, 25.5 per cent. of the total nitrogen in the urine. According to Amberg and Morrell[6] the uric acid nitrogen as compared with total nitrogen is about 3 per cent.

September 16. The general condition was about the same. The coagulation time was seven minutes.

September 17. Blood examination: Hemoglobin, 110 per cent.; red blood cells, 6,248,000; white blood cells, 17,000. The coagulation time was now prolonged to twenty-five minutes. There were no hemorrhages.

September 18. The child's general condition was not good. The temperature was from 101° to 103°. Pus discharged from both ears. Bleeding started from the mouth, finger tips, and transfusion wounds. The icterus was much more pronounced.

September 19. The general condition was very poor. The temperature 104°. The hemorrhages continued and the stool contained blood. Blood examination: Hemoglobin, 105 per cent.; white blood cells, 12,000; coagulation time, three hours.

September 20 and 21. Child's condition steadily grew worse. Hemorrhages continued. A hemorrhagic vesicular eruption developed. High fever.

September 22. Died, eight days after transfusion. No autopsy was permitted.

The most important facts thus far brought out in this case are: (1) The mother's history of miscarriages (syphilis?); (2) the child nursed at a suppurating breast; (3) the late date (seven days) at which the hemorrhages began; (4) the blood failed to coagulate; (5) the marked temporary effect of the transfusion; (6) reappearance of the original symptoms and progressive loss of the coagulating power; and (7) the child did not die exsanguinated.

[3] Jahr. f. Kinderheilk., 1893, xxxv, 21. Stoffwechsel des Kindes.
[4] Zeit. f. Geburtsh. und Gynäkol. xxxiii.
[5] Yahr. f. Kinderheilk., 1909, p. 288.

CASE II.—*Multiple hemorrhages; prolonged coagulation time; congenital syphilis; sterile blood culture.* Baby H., male, four weeks old. First seen on December 27, 1908. This is the mother's first child; normal birth; breast fed. Father has had syphilis. For the last week the child has been bleeding from the nose (both nares, principally the right). For the last two days he has vomited blood. Yesterday his stools were tarry.

Physical Examination. Small, weazened, extremely pale infant; frontal bosses prominent, fontanelles large, no craniotabes; dilated veins over scalp. Blood discharging from both nostrils; a few hemorrhagic spots on the palate. Desquamation of skin of hands and feet. Heart: Systolic murmur heard all over the chest. Lungs: Rales over both chests. Abdomen distended; superficial veins dilated. Liver palpable at level of umbilicus, smooth. Spleen palpable three finger-breadths below free border of ribs. Blood smears showed: Polynuclear cells, 62 per cent.; eosinophiles, 1 per cent.; mononuclear, 37 per cent.

The coagulation time showed very marked delay; after five hours a few threads of fibrin had formed. Coagulation experiments done with this blood are described below.

A blood culture was obtained in the following way: A compression bandage was put around the thigh to produce hyperemia of the lower extremity; the foot was thoroughly disinfected and the skin pierced with a Hagedorn needle; the drops of blood were collected in ammonium oxalate solution. Three cubic centimeters of blood collected in this way, and subsequently plated out in agar and glucose agar, remained sterile.

Bleeding from the needle wound as well as from the nose continued until the child's death, which took place eight hours after the child was first seen. The period of observation was so short that more clinical facts could not be brought out.

Autopsy, twelve hours post mortem: Heart muscle pale; lungs show no pneumonia; spleen enlarged, firm; liver large, heavy, light yellow. Intestines show nothing abnormal. Cerebrospinal fluid consisted of dark blood, increased in amount, and under considerable pressure.

A positive Wassermann reaction for syphilis was obtained with this fluid, by Dr. Noguchi, of the Rockefeller Institute.

Microscopic sections showed in the liver the pericellular inflammation characteristic of congenital syphilis. With the Levaditi method numerous Spirochætæ pallidæ were demonstrated in the liver, but not in the other organs. The spleen was considerably enlarged and showed a general hyperplasia microscopically.

THE DIAGNOSIS OF HEMORRHAGIC DISEASES IN INFANTS. In discussing the diagnosis of these two cases it is necessary to keep in mind that the hemorrhagic disease of the newborn is not one disease, but is a symptom which may be due to a number of

different causes. All the cases, however, which ought, strictly speaking, to be included under the name "the hemorrhagic disease of the newborn" have two characteristics in common: (*a*) The bleeding is uncontrollable, and (*b*) the blood coagulates very slowly or not at all.

Finkelstein[7] divides these cases, clinically, into two varieties: (1) Cases of multiple hemorrhage; and (2) cases of hemorrhage from one place only.

1. Cases of multiple hemorrhages from surfaces and internal organs generally show severe febrile symptoms and are often due to some form of infection. Their bacteriology is not very well established, as nearly all of the cultures have been obtained post mortem only. Babes "bacillus of hemorrhagic disease" and the bacillus isolated by Kamen in an epidemic of Winckel's disease have not been found by other observers. Two special clinical varieties of disease with multiple hemorrhages have been described. In the one known as Buhl's disease the hemorrhages are accompanied by cyanosis and icterus, but no fever; a marked fatty degeneration of the organs is characteristic. The second variety, known as Winckel's disease, occurs usually in epidemics in institutions; besides the hemorrhages there are icterus and hemoglobinuria. Among the very rare causes of multiple hemorrhages in infants are congenital stenosis of the bile ducts, cirrhosis of the liver, leukemia, and pseudoleukemia. Congenital syphilis may cause either multiple hemorrhages or bleeding from one point. The question whether syphilis alone is the cause of the hemorrhages in these cases, or whether there is a complicating general infection, has been much discussed. Finkelstein believes from a study of seven cases that the hemorrhages are always due to a secondary bacterial infection. He says "a true syphilis hemorrhagica of the newborn does not exist."

Our second case, in which a sterile blood culture was obtained, seems to indicate that bacteremia does not necessarily occur in this class of cases. That a local infection in the nose may have existed in this case cannot be denied. Yet in view of the loss of coagulability this cannot be regarded as the immediate cause of the continued bleeding. That toxic absorption from such a local lesion may be the ultimate cause of the loss of coagulability, is possible.

2. Cases of hemorrhage from a single region, with certain possible exceptions, are probably due to the same causes as multiple hemorrhages. The bleeding in some cases is connected with a local infection at the bleeding point. The most common sources are the umbilicus and the intestines.

Umbilical hemorrhage usually comes from the stump of an infected cord and begins during the first or second week of life. It is generally a slow oozing, and may last for hours or days. It is

[7] Säuglingskrankheiten.

usually not a fatal affection. We have no data upon the question of coagulation of the blood in these cases.

Hemorrhage from the bowels in infants may be due to a variety of causes. "Melena neonatorum idiopathica" is a term applied to those cases which cannot be ascribed to syphilis, sepsis, or a local lesion. It usually commences before the fourth day of life, and is generally, but not invariably, fatal. Vaginal hemorrhage in infants is very rare; of seven cases collected by Ritter, four were due to septic infections. Nasal hemorrhage is most commonly due to syphilitic rhinitis. Hemophilia naturally suggests itself as a possible cause of hemorrhages in the newborn—especially in view of the fact, now well-established, that in hemophilia also the coagulating power of the blood is much impaired. As a matter of fact, however, hemophiliacs very rarely begin to bleed in the first few months of life, and when they do the hemorrhages are seldom fatal.

Before the blood changes were known the hemorrhagic diseases were often ascribed to lesions of the vessel walls. More recent work has cast much doubt on this, though it is still regarded by some as a possible contributing factor. In considering the etiology of the two present cases, we must ascribe the first case to a general infection, probably derived from the mother's breast, the second to congenital syphilis.

The Physiology of Blood Coagulation. In spite of the enormous amount of work that has been done on the physiology of coagulation, that subject is not yet clearly understood. There are many important facts, however, on which there is practical agreement. It has, of course, been known for many years that fibrin ferment, which acting on fibrinogen forms fibrin, does not exist in the circulating blood, but is formed from at least two preëxisting substances, and this only in the presence of a third substance, calcium ions.[8] Of the two preëxisting substances, the one, generally called prothrombin, is probably (though by no means certainly) present in the plasma. The other, thrombokinase, the activating substance, is never present in the circulating blood, but is only produced from certain nucleated cells (and according to Morawitz[9]), chiefly from blood platelets. Large amounts of thrombokinase can be extracted from certain very cellular organs, such as thymus, testis, liver, kidney. The coagulation of the blood in wounds is much hastened by the thrombokinase at once liberated from the injured tissue cells.[10]

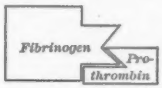
When fresh clot or serum is examined, it is always found to

[8] Arthur and Pages, Archives de Physiol., 5, ii, 12; Hammarsten, Jour Physiol., 8; Zeitschr. f. physiol. Chem., 22.

[9] Deutches Archiv f. klin. Med., 79.

[10] Rettger (Amer. Jour. Physiol., July. 1909, p. 406), has made certain objections to the thrombokinase theory. We have repeated some of his experiments and believe that by a modified technique Rettger has obtained a very pure fibrinogen, nearly or quite free of prothrombin, and therefore not coagulable by kinase alone.

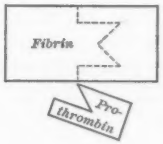
contain free fibrin ferment. Why, then, does not clotting continue to extend indefinitely up the lumen of a vessel, in whose open mouth a clot has formed? This (as well as many other apparently contradictory phenomena) is explained by the antifibrin ferment whose presence in normal blood has only recently been recognized.[11] This antifibrin ferment is present in large excess and (in the course of hours) neutralizes any fibrin ferment present in serum. It does not



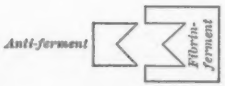
1 Represents the normal state of prothrombin loosely attached to fibrinogen (Mellanby).

2 Represents the elements necessary to the formation of fibrin ferment.

3 Represents fully formed fibrin ferment.



4 Represents the action of fibrin ferment on fibrinogen to form fibrin and the liberation of the prothrombin which was associated with the fibrinogen. This prothrombin, with the kinase, which is usually formed in excess, forms the free fibrin ferment which is always found in perfectly fresh serum.



5 Represents free antifibrin ferment.

6 Represents fibrin ferment neutralized by the antifibrin ferment.

A scheme to illustrate the relationships believed to exist among the substances involved in coagulation. (Based on the theories of Mellanby and of Morawitz.)

affect kinase or prothrombin, but only fully formed fibrin ferment. It has less affinity for fibrin ferment than fibrinogen has (otherwise clotting would never occur at all).

The accompanying diagram may help to make the relations of

[11] Mellanby, Jour. of Physiology, 1, 1909; Morawitz and Jossen, Deutches. Archiv f. klin. Med., 1908, xciv, 111.

these substances clear. It should be understood that the diagrams represent merely relationships, and that nothing is implied as to whether the substances unite with each other as chemical entities.[12]

PATHOLOGICAL CHANGES IN COAGULATION. In the disease under discussion the essential change in the blood is impaired coagulability. It is worth considering the things which may produce this condition experimentally or which might be conceived to cause it pathologically.

1. *Total Absence or Diminished Amount of Fibrinogen.* In the absence of fibrinogen, of course no coagulation can occur. Experimentally, numerous observers have found that various things which destroy liver parenchyma cause the blood to become uncoagulable, due to absence of fibrinogen.[13] The condition has never been known to occur clinically. As to a diminished amount of fibrinogen, one of the most interesting points brought out in Mellanby's recent study of the physiology of coagulation is that increasing the amount of fibrinogen actually lengthens the coagulation time (that is, the time for the formation of a definite amount of fibrin), and conversely, diminished fibrinogen means shortened coagulation time. This, if true, seems to us to offer at least a partial explanation of the much shortened coagulation time seen usually in severe hemorrhages (when a considerable portion of the fibrinogen in the body may be lost).

An experiment performed in each of the cases described in the present paper showed conclusively that there was enough fibrinogen present in the blood to cause the formation of a normal clot. To a large drop of the infant's blood, which had not clotted after several hours, was added as much normal blood (from the finger) as could be carried on the point of a pin. Coagulation always occurred in from two to four minutes.

2. *The Absence or Diminution of Calcium.* While the presence of dissolved calcium salts is absolutely essential to the formation of fibrin ferment, there is some question whether calcium is ever diminished to such an extent as to cause pathological interference with the coagulation. Recent work[14] has cast much doubt on the therapeutic value of calcium in hemorrhagic conditions. In both of the present cases experiments were performed to determine whether lack of calcium was the cause of the interference with coagulation. Small amounts of dilute calcium chloride (0.1 to 1 per cent.) were added to drops of the blood. No coagulation occurred. It therefore seems probable that in these cases the failure to coagulate was not due to lack of calcium.

[12] On this question, and for the researches on which the present abstract is founded, see Bayliss, The Nature of Enzyme Action, 1908, p. 73; Mellanby, loc. cit.; Morawitz, loc. cit., and Ergebnisse d. Physiol., 1905, 4, 307; Pekelharing, Biochem. Zeitschr., 1908, 11, 1; Wolf, Arch. Internat. de Physiol., 1906 and 1907.

[13] Doyon, Comptes rendus Société de Biologie, 1905, lviii.

[14] Addis, Quarterly Jour. Med., January, 1909.

3. *The Absence of Prothrombin.* There is no evidence as to whether this ever occurs in disease. It is said to be brought about by experimental phosphorus poisoning.[15]

4. *The Absence or Diminution of Thrombokinase.* That different tissues and cells vary widely, some liberating large amounts of thrombokinase, others almost none, is well known. There is no direct experimental proof that the quantity of kinase that can be obtained from a given tissue varies under physiological or pathological conditions.

Sahli,[16] in 1895, first suggested that the disease hemophilia might be due to deficiency of thrombokinase—a definite ferment anomaly of all the body cells. Recently Morawitz and Lossen[17] have practically proved this—have shown that in hemophilia the prolonged coagulation of blood drawn directly from the veins is due to deficiency of kinase, and Morawitz and Bierick[18] have proved the same in the prolonged coagulation of cholemia.

An experiment performed with the blood of the first case described in this paper proved that absence of thrombokinase might have been the factor. A drop of ascitic fluid was added to a drop of the blood. No coagulation occurred.

Now serous fluids are said to contain all the elements necessary to coagulation except kinase; they have no cells which can give rise to kinase, and they, therefore, coagulate on the addition of kinase alone (Mellanby). It follows that in the experiment done, if the child's blood had contained kinase, coagulation should have occurred.

While too much should not be inferred from a single experiment, particularly as no control experiment was done to show that the specimen of ascitic fluid used would coagulate on the addition of kinase, nevertheless, the experiment does seem to narrow the possibilities to two: either thrombokinase was absent, or some pathological, inhibiting substance was present.

5. *Coagulation Inhibiting Substances.* Many of the substances which can prevent coagulation experimentally, such as hirudin, snake venoms, acids and alkalis, and substances like oxalates, citrates, and fluorides, which act by precipitating calcium, do not need to be considered in the present connection. It is interesting that exceedingly small amounts of some of these substances are enough. Thus, hirudin (Merck) prevents 7000 times its own weight of blood from coagulating.

(*a*) *Bile.* Bile salts in the test-tube not only prevent the action of formed fibrin ferment, but prevent its formation; this, however, only happens in such concentrations (0.5 per cent.) as never occur

[15] Doyon, Comptes rendus Société de Biologie, 1905, lviii, 852; Corin and Ansisus, Vierteljahrsschrift f. gerichtliche Medizin, iii, 434 (quoted from Morawitz and Bierich, loc. cit.).

[16] Zeitschrift f. klin. Med., i, 264.

[17] Deutsch. Archiv f. klin. Med., 1908, xciv, 111.

[18] Archiv f. experiment. Pathol. u. Pharmakol, lvi, 115.

in the body blood.[19] Furthermore, it is well known that the tendency to hemorrhage is independent of the degree of icterus, and, indeed, the hemorrhages sometimes occur after the icterus has disappeared. These facts indicate that it is not the mere presence of bile in the blood that causes cholemic hemorrhages. Exactly what does cause the interference with coagulation in these cases is unknown; but Morawitz and Bierich have advanced our knowledge one step by showing that whatever the toxic substance is, it acts by preventing the secretion of thrombokinase.

That the same factor may have been at work in the two cases under discussion is possible; in the first there was only a moderate jaudice, but destruction of liver cells was the most marked lesion in the body.

(*b*) *Peptone.* It has been known for a long time that the injection of peptone or albumose into the circulation retards or prevents coagulation. Delezenne,[20] in 1898, showed that if peptone is circulated with blood through a living liver, not only will the blood itself not clot, but it will prevent clotting if added to the freshly drawn blood of another animal. The peptone evidently acts, then, by inducing the formation of some coagulation-inhibiting substance in the body. It is known that traces of peptone are occasionally found in the blood in leukemia,[21] and it seems to us that this may possibly have some connection with the delayed coagulability and the tendency to hemorrhages so often seen in some forms of leukemia. In the absence of any evidence to the contrary, this also may be tentatively regarded as one of the possible causes of the condition of the blood in the disease under discussion.

(*c*) *Acids.* The influence of acids on coagulation is very great. Mellanby finds that $\frac{1}{5000}$ normal hydrochloric acid delays the onset of coagulation, and $\frac{6}{10000}$ normal hydrochloric stops it. He states that the importance of the observation lies in its application to the non-coagulable state of the blood which often accompanies acid intoxications.

It seems to us, however, that the inference should be very cautiously accepted. In Mellanby's experiments the reaction was actually acid, whereas it is well known that in no form of acid intoxication does the reaction of the circulating blood ever become acid. Furthermore, the most common clinical types of acid intoxication are not accompanied by loss of blood coagulability.

(*d*) *Products of Autolysis.* In 1902 Conradi[22] published the results of experiments in which he proved that coagulation-inhibiting substances of unknown nature, to which he gave the name "antithrombin," were produced in the aseptic autolysis of organs. These substances are evidently entirely different from the antifibrin

[19] Morawitz and Bierich, loc. cit.
[20] Travaux de Physiologie, Universite de Montpellier, 1898.
[21] Erben, Zeitschr. f. klin. Med., 1900, 282.
[22] Hofmeister's Beiträge, 1902, i, 136.

ferment of normal serum because they are not injured by boiling, whereas the antifibrin ferment of serum is completely destroyed by 70° C. for a few minutes.

In Conradi's experiments intravascular injection of these products of autolysis did not produce any very marked effects. Nevertheless, it is conceivable that substances of this nature might be absorbed and cause delayed coagulation in the body.

With regard to the question of an inhibiting substance in the two cases described in this paper, the experiments described above indicate that there was no coagulation-inhibiting substance in the blood, but that if any inhibiting substance was present it must have been a substance capable of preventing the formation of fibrin ferment, but not the action of the latter after it was once formed. For in both of the cases the addition of an exceedingly small (though, we regret, not accurately measured) proportion of blood from any normal person caused clotting in approximately the time required for the coagulation of normal blood.

THERAPY. We do not intend to enumerate the various measures which have been tried in the hemorrhagic disease of the newborn. In Case I, calcium chloride was administered, with no effect on the coagulation. From the experiment described above no effect was actually to have been expected from this treatment.

In Case I, also, a subcutaneous injection of 20 c.c. of horse serum (not fresh) was given; there was no effect either on the coagulation time or the clinical symptoms.

The use of serum by subcutaneous or intravenous injection in the treatment of hemorrhagic conditions due to diminished coagulability is new,[23] and its value is still sub judice. Many favorable cases have been reported.[24] Most of these are rather unsatisfactory, as they are simply reports of recoveries after serum injections, in conditions many of which are recovered from spontaneously. Weil, who first used the serum treatment, studied his case of hemophilia carefully; he found that there was marked shortening of coagulation time after intravenous injections of serum; this remained for about a week, and was only completely lost after five weeks. He does not state how old his serum was. All the recent writers insist that the serum must be fresh, on account of the well-known disappearance of fibrin ferment from serum on standing.

Nevertheless, the expectation that the injection of serum will alter the coagulating power of the circulating blood runs so contrary to our physiological data that we prefer to remain skeptical as to the value of this form of treatment. The considerations which lead us to this point of view are as follows:

[23] P. Emile Weil, Presse médicale, October 18, 1905.

[24] Broca, Medizinische Klinik., 1908, p. 1445; Carrière, Münch. med Wochenschr., 1907; Lommel, Centralbl. f. innere Med., July, 1908; Leary, Boston Med. and Surg. Jour., July, 1908; Welch, Amer. Jour. Med. Sci., 1910, cxxxix, 800.

The injection of large amounts of fibrin ferment into the circulation causes extensive intravascular clotting, and often death. This is the chief reason why the old method of transfusion by the injection of defibrinated human blood was given up.[25] And it has been repeatedly shown that intravascular injection of small amounts of thrombokinase causes death rapidly with multiple thrombi.[26] In other words, the actual presence of fibrin ferment in the circulating blood is very dangerous.

On the other hand, the injection of moderate amounts of fibrin ferment gives no trouble, because (as we now know) the fibrin ferment is rapidly neutralized by the excess of antifibrin ferment in the blood. A considerable quantity of very active fibrin ferment may be injected into the blood current of a living animal without producing clotting at all.[27] This is the reason that there have been no fatalities following the intravenous injections of serum. The difficulty with the serum treatment, then, from a theoretical standpoint, is that the fibrin ferment contained in an ordinary dose (10 to 30 c.c.) of serum is at once neutralized by the antifibrin ferment of the circulating blood.

There is nothing to show that fibrin ferment, once it is neutralized by antiferment, can be subsequently liberated. It is, of course, conceivable that the elements of fibrin ferment may be picked out and subsequently used in the production of prothrombin and thrombokinase by the cells which produce these substances. This would afford a rational explanation of the serum treatment.

The studies on the serum treatment have been almost entirely clinical. Recently, however, Baum[28] has reported on experiments with rabbits whose blood was made uncoagulable or only slowly coagulable by hirudin injections. In cases in which the coagulation was merely prolonged he found that blood withdrawn at once (five to ten minutes) after a serum injection coagulated somewhat more rapidly. When enough hirudin was given to make the blood uncoagulable, the serum had no effect at all.

At the same time Baum reported on three cases of hemophilia. In two of these serum injections were absolutely without influence. In the other case they seemed to have some, though slight, effect. We would like to add that we have seen two hemorrhagic cases (of jaundice) in which the injection of fresh serum was futile.

What has been said does not apply, of course, to the local application of fibrin ferment, in the form of serum, to the bleeding point.

We have one other therapeutic measure to consider. Transfusion, since Crile re-introduced it, has been used successfully in many hemorrhagic cases, particularly in those due to prolonged jaundice.

[25] Landois, Die Transfusion, 1875; Billroth, Die Transfusion, etc., 1886.
[26] Conradi, loc. cit., p. 166.
[27] Foster, Text-book of Physiology.
[28] Mittheilungen a. d. Grenzgebeit, etc., 1909, xx, 1.

Recently its succesful use in a case of hemorrhages of the newborn has been reported.[29]

Transfusion not only replaces the lost blood, but stops the hemorrhages by supplying new material for the production of fibrin ferment, as was seen in the case described above. Transfusion does not, of course, remove the original cause of the disease. This also is well illustrated by our case, in which, as the underlying septic condition continued, the coagulating power of the new blood also was gradually destroyed.

Conclusions. 1. Impaired blood coagulation is the immediate cause of uncontrollable hemorrhages in the newborn.

2. This is probably due to destruction of, or interference with, the production of thrombokinase.

3. Bacterial infection is the most frequent underlying cause of the disease; but

4. Syphilis alone can cause the disease without bacterial infection.

5. The value of serum injections is doubtful.

6. It is important that transfusion should be tried when ordinary measures have failed.

THE RADIOGRAPHIC DIAGNOSIS AND CLASSIFICATION OF EARLY PULMONARY TUBERCULOSIS.

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It is acknowledged by nearly all physicians that in making the early and positive diagnosis of pulmonary tuberculosis lies the only hope of permanent cure. Much time and energy have been expended in the search for a specific when the specific was at hand and free to all, and very positive in cases in which the diagnosis is made as early and positively as it may be made by radiographic examination.

Symptomatology. If pathology is the foundation of all diseases, then symptomatology is the superstructure that we all see and feel and causes the patient to consult the physician. The subjective symptoms vary extensively on account of the observation of the patient and his methods of description, and there are great variations of symptoms caused by similar pathological lesions. Leading questions are asked by the physician, and some will record one symptom and some another. The history often resembles the physician who records it, rather than the patient who makes it.

Objective Symptoms. Objective symptoms depend very largely on the observations of the physician. Routine examination will

[29] V. Lambert, Medical Record, May 30, 1908.

often improve one's power of observation, but a "Sherlock Holmes," though a layman, may observe many symptoms that escape the attention of even a trained "Dr. Watson," but the careful observer may not be able to attribute the proper value to the symptoms.

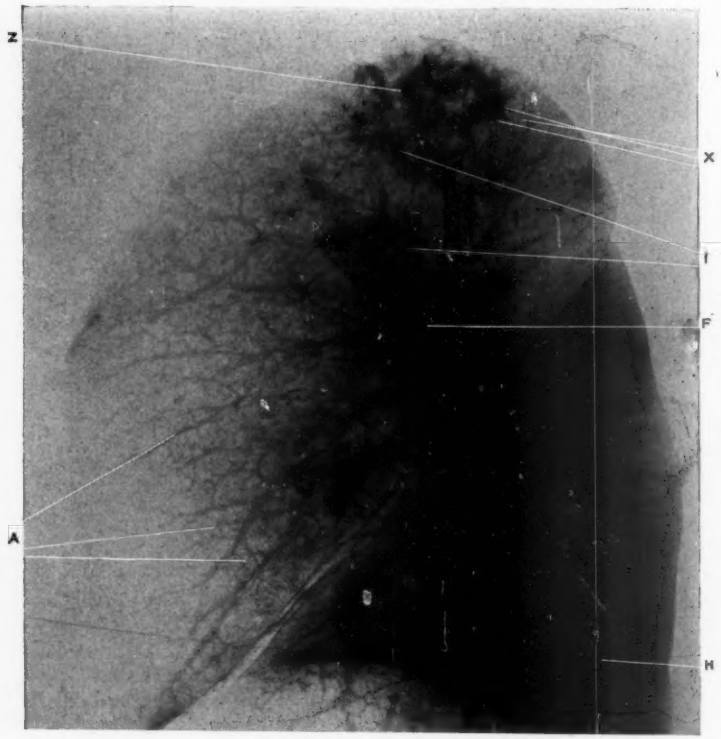


FIG. 1.—Radiogram of a lung which had been removed from the body and inflated to about the normal extent. The lower lobe shows the earliest stage of congestion, preceding a pneumonic process which had extended from the opposite side. *A*, normal markings of the lung; *F*, thickening around the root; *I*, old calcified tubercles. The apex shows infiltration, and isolated (*X*) and conglomerate (*Z*) tubercles, and (*H*) consolidation. This figure shows about the same detail which one is able to obtain in a favorable living subject.

HEMOPTYSIS. Hemoptysis is such an important symptom that it deserves special mention. It may be one of the first symptoms of acute infection, or it may be caused by old calcified tubercles scratching through the bronchial membrane (Fig. 20, I).

PHYSICAL SIGNS. Very closely associated with the objective symptoms are the physical signs. They have been, and always will

be, the sheet anchor of pulmonary diagnosis; and on account of its being a tool that every physician has, it should be used to its utmost capacity. I have made several series of radiograms of cases that had previously been examined by some of the most eminent physical diagnosticians in New York, and I think that all of them admit the value of the *x*-rays. Some of them rely very largely on the radio-

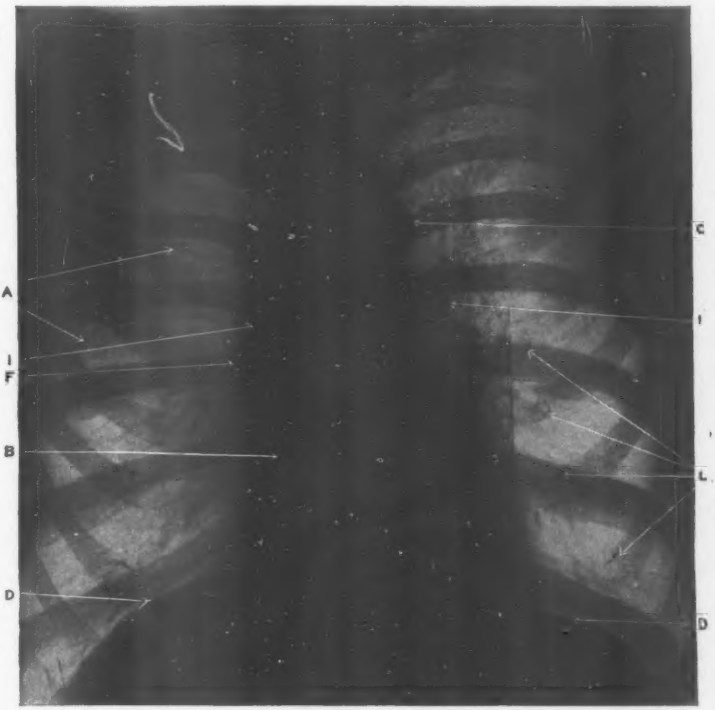


FIG. 2.—Radiogram of a lung which is as nearly normal as any I have ever seen, and shows the followng detail (both lungs being equally aërated): *A* normal markings of the lungs; *B*, border of heart, shows distinctly, normal in size, shape, and position; *D*, dome of diaphragm; *F*, root of lung; *I*, calcified tubercles; *L*, calcified costal cartilages. It is possible to obtain this detail in a patient of moderate size, when the aëration of the lung is complete.

graphic findings to determine whether radical treatment is necessary in border line cases; and one of the most eminent diagnosticians has modified his interpretation of the physical signs, especially the "harshness of breath sounds."

Physical signs may be divided into distinct classes: (1) Those which are directly the result of tuberculous infiltration, such as, dulness, increased fremitus, and changes in voice and breathing. These

are the real physical signs of tuberculous infiltration and consolidation, and naturally do not occur until the process has passed out of the stage of incipiency. (2) The physical signs on which the diagnosis of incipient tuberculosis is based, such as slight localized rales, or "clicks," as they are sometimes called; these are not the physical signs of infiltration or consolidation, but the signs of a localized pleurisy or bronchitis which may or may not be of tuberculous origin. On the other hand, this localized bronchitis or pleurisy may not occur until the tuberculous process has reached

FIG. 3.—Symptoms were classical of a tuberculous process. Physical signs indicated an incipient lesion at the left apex; the right apex was *normal*. There was diminished aëration of both apices; the heart was normal in size, shape, and position; the diaphragm is not shown. *F*, thickening around both roots, typically tuberculous; *G*, infiltration of both apices with large, soft, isolated (*X*) and conglomerate (*Z*) tubercles, indicating an exudative type of infection. The process is a little more advanced on the left side, where the physical signs were found, but more extensive in the right, where there were no physical signs. *X*, isolated tubercles; *Z*, conglomerate tubercles.

such an advanced stage that it is accompanied by dulness and increase of voice and breathing, and by that time the process has reached a stage in which pathologically or radiographically it could not be considered in its incipiency.

About once in three or four times, in equivocal cases, we find a patient in whom the bronchitis has not developed, or at least has not been discovered, until the infiltration is well marked radiographically, and yet the process has not reached a stage that will give dulness or increase in voice or breathing. This is especially true when the

process is a direct extension from the root or is located posteriorly under the scapula.

I have been criticised for stating that certain plates showed individual miliary tubercles. That there may be no misunderstanding of the term "miliary tubercles," I quote the definition of miliary tubercles from Delafield and Prudden:[1] "Miliary tubercles are small nodules of irregularly spheroidal shape, the smallest hardly visible to the naked eye, the largest as large as a pea." "The term miliary tubercle, which arose from the crude coincidence in size between small foci of tuberculous inflammation and some forms

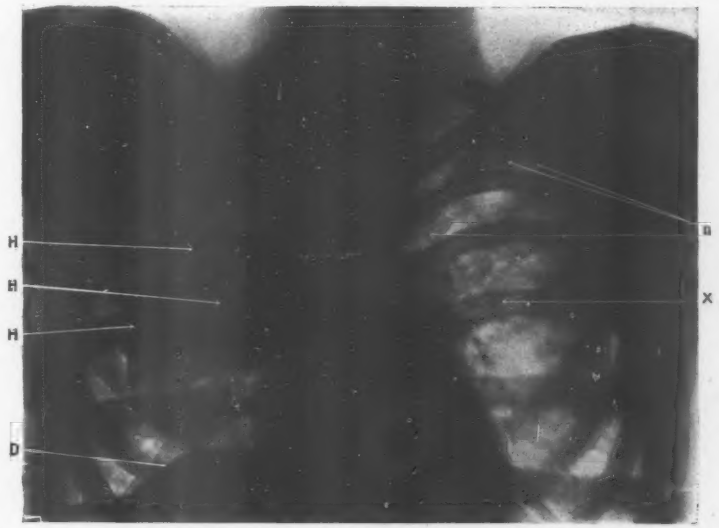


FIG. 4.—The symptoms and physical signs were classical in this case, and there were tubercle bacilli in the sputum. The plate is shown only to illustrate a typical exudative process in the stage of consolidation. There was diminished aëration of both lungs. The heart was normal in size, shape and position. *D*, diaphragm retracted on the right side (Williams' sign); *G*, infiltration of the left lung; *H*, three small areas of complete consolidation of the right lung; *X*, isolated tubercles in the left lung.

of millet seeds, is now liberally applied to tubercles which are much larger as well as those which are much smaller than millet seeds."

In speaking of miliary tubercles, I refer to those of moderate size, which on cross section of the lungs appear as grayish-white nodules about the size of a pin head. Pathologically these are composed of exudate or productive tissue in a number of adjoining air cells. In studying them radiographically they are compared

[1] Pathology, p. 216.

in density with the air which should normally fill those cells, instead of tissue of similar density, as is the case in tuberculous infection in any other part of the body. This is the reason why individual tubercles show in the lung and not in any other tissue in the body. It is universally admitted that the larger necrotic and calcareous tubercles show; I do not claim to show the microscopic ones. But it is the intermediate tubercles, the smallest ones that are clearly discernible by the naked eye on the cross section, those that give the "shotty" feeling to the cut surface of the lung, that show distinctly in a radiogram having sufficient detail. It is on these tubercles that the positive diagnosis of incipient pulmonary tuberculosis by the *x*-rays depends.

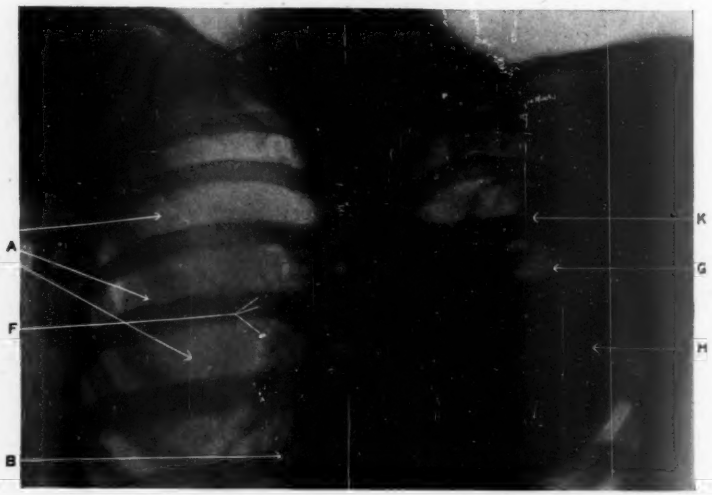


FIG. 5.—Is one of a patient with typical symptoms of pulmonary tuberculosis. Physical signs indicated only a slight involvement. The radiogram, however, showed the following detail: *A*, normal markings of the lungs show fairly distinctly; *B*, heart normal in size, shape, and position; *F*, typical mottled infiltration around the right root, which is the only indication of infection on the right side; *G*, infiltration of the middle of the left lung, below which the process has reached the stage of consolidation (*H*), and above which is a cavity (*K*) about 3 cm. in diameter.

SPUTUM EXAMINATION. The diagnosis is absolutely positive if the tubercle bacilli are found in the sputum, but they are usually not found until physical signs have developed and the disease has passed out of the stage of incipiency. One is certainly not justified in waiting until they are found before making a diagnosis.

TUBERCULIN TESTS. The tuberculin tests are the greatest aid in determining the presence of a tuberculous process somewhere in the body. It is manifestly not within the scope of this paper to

discuss the dangers and value of these tests except as compared with radiography.

Von Pirquet states that during a year and a half he made a cutaneous test on all the children who were admitted to the children's clinic of Professor Escherich in Vienna, and that 93 per cent. of the children, fourteen years of age, reacted to the tests, and in only 13 per cent. was there manifest tuberculosis. This corresponds so accurately with the radiographic findings that it would be interesting

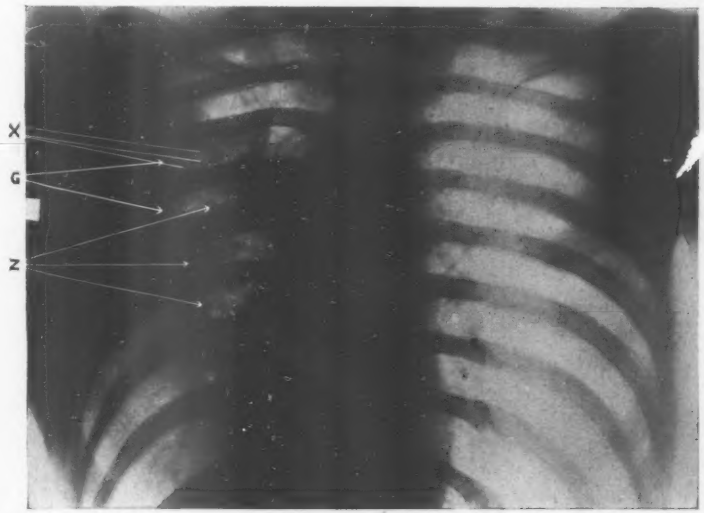


FIG. 6.—Posterior view of the same patient as shown in Fig. 5; the cavity, being nearer the anterior wall of the chest, does not show in this figure. The infiltration has not reached the stage of consolidation posteriorly, but shows the typically mottled appearance of a tuberculous infiltration, (*G*); *X*, small, isolated tubercles; *Z*, large, conglomerate tubercles.

to know what part of the 87 per cent. that showed no manifest lesion would have shown a distinct lesion around the root of the lung on radiographic examination. Unfortunately the tuberculin tests do not show the activity, location, or extent of the lesion.

The search for a specific which has resulted in the tuberculin tests led out of the rut of symptomatology and physical diagnosis, opened up a new field of laboratory tests, and created a demand for more accurate methods of diagnosis.

The Röntgen rays presented themselves as a candidate before the technique of making radiograms was perfected; attempts were made to use them either fluoroscopically or radiographically in the diagnosis of pulmonary lesions, and much was claimed for them that could not then be substantiated. The whole field of Röntgen-

ology savored just enough of the magic art to be a fertile field for fakirs and charlatans. Many physicians who had failed in other branches of medicine flocked into this without any instruction or experience; and many of them did not know the first principles of electricity or photography, and only a moderate amount of medicine. Some general practitioners, with little or no experience, would look

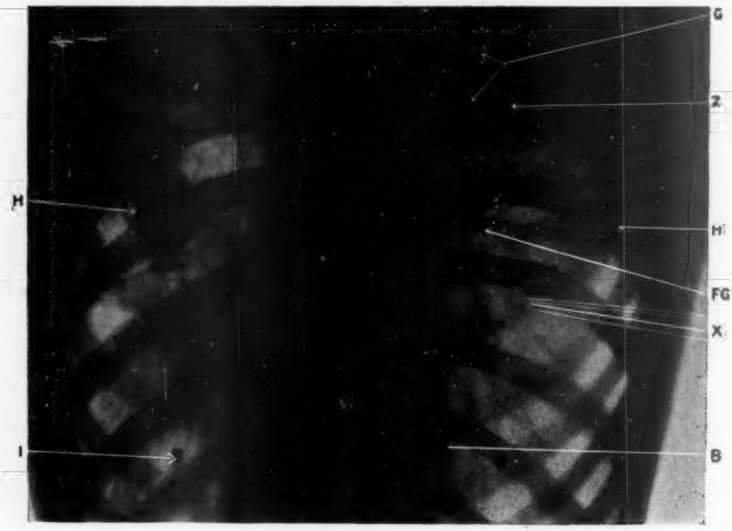


FIG. 7.—This case was radiographed to show an œsophageal stricture; although there were slight physical signs, they were not considered of importance. Radiographic findings: Diminished aëration of the entire right lung and left apex; *B*, heart is drawn into the vertical position—Hickey's symptom; *F G*, thickening around both roots; *G*, tuberculous infiltration of both lungs, more advanced on the right side, behind. The lesion in the right apex illustrates a typical subacute productive process as indicated by infiltration (*G*); *H*, small areas of consolidation in both lungs; *I*, isolated, calcified tubercles; *X*, isolated fibrous tubercles; *Z*, conglomerate tubercles.

in a fluoroscope and claim to see things that an experienced operator knew could not be seen; while others would make radiograms of advanced lesions that could readily be diagnosticated by other methods.

During the evolution of Röntgenology its advocates were divided into two camps—those who favored fluoroscopy, and those who favored radiography; strange as it may seem, few were successful with both methods. The Austrians are the most ardent supporters of the fluoroscopic method. Dr Williams, of Boston, is one of the greatest devotees in this country, and Dr. Minor,[2] of Ashville, Tenn., has just written an article on this method of chest examination. The advantages of this method, as enumerated by Dr. Minor, are as

[2] The American Treatise on Tuberculosis, edited by Arnold Klebs.

follows: Fluoroscopy is much less work, can be done by any general practitioner who has a static machine or small coil, only requires one tube which may be used for any number of exposures, and is, therefore, much less expensive. There are no plates to be developed, and it does not show the normal markings of the lung, which he says are so confusing to one unfamiliar with such examination.

Dr. Minor states that tuberculous processes are detected about as soon by this method as by a keen physical examination. He admits that radiograms may be made that show a tuberculous process much earlier than can be shown fluoroscopically or by physical examination, but he also says that such radiograms must be made and interpreted by one who is experienced in this line of work. I believe all his points are well taken, but would call attention to the following disadvantages of fluoroscopy: The risk to the operator is too important to be disregarded; he has only the impression gained from a few seconds, or minutes at most, and the personal equation of what he sees and what he does not see is an important factor. Only the grossest and more advanced lesions may be diagnosticated by this method.

The advantages of radiography are as follows: Radiograms may be made without risk to the operator or patient; one has a permanent record which he may study at leisure and compare with radiograms of similar cases, and save to compare with radiograms made at a later stage, to show whether the process is advancing, held in check, or resolving, and many of the cases do resolve. A radiogram may also be used to persuade a patient, who has few symptoms or physical signs, that radical treatment is necessary.

Dr. Minor says the radiogram gives such a wealth of detail that it is confusing and difficult of interpretation, and therefore, the fluoroscopic method is better. It seems just as rational to discard the high power microscope because of the increased detail it gives. It is just the interpretation of this wealth of detail that enables one to make the diagnosis of tuberculosis by radiographic examination very much earlier than by fluoroscopic methods or physical diagnosis.

Rieder in Europe (Munich) and Hulst in America (Grand Rapids, Mich.) were the pioneer workers in rapid radiography of the chest, and much credit is due them; but both used the high vacuum method that does not combine the wealth of detail with the contrast that can be obtained with the low vacuum tube advocated by Leonard.

The following factors are important in the development of soft tissue radiography. (1) The perfecting of the apparatus that enables one to make radiograms of the chest while the patient holds the breath, or even during the diastole of the heart. (2) The improvement in technique, especially as regards the separation of the direct, indirect, and secondary or Sagnac rays.[3] (3) The selection of a tube suitable for the apparatus used and the seasoning of

[3] Archives of the Röntgen Ray and Allied Phenomena, May, 1905. Archives of Physiological Therapy, December, 1906.

that tube so that it generates a large percentage of direct rays and enables one to make radiograms that show distinctly the muscle, fat, connective tissue, and even the blood in the veins at the anastomosis

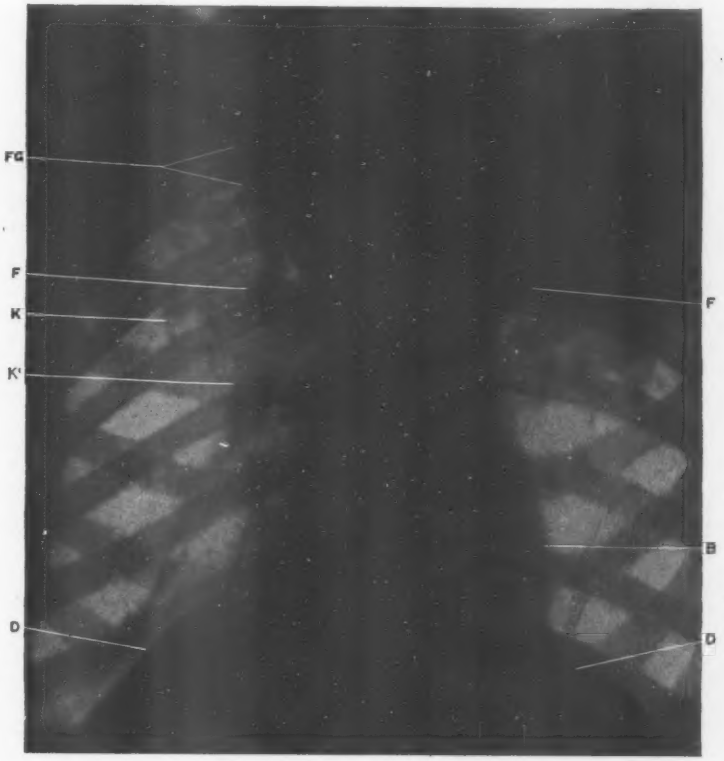
FIG. 8

FIGS. 8 and 9.—This is a test case to compare the relative value of radiography and physical who found signs of consolidation at the left apex, but made a negative diagnosis of any more marked on the left than on the right; *B*, heart drawn into the vertical position *H*, consolidation of the left apex, more marked behind; *FG*, infiltration of the right upper with exudate; *K*, bronchiectasis, empty. It would hardly seem possible for a tuberculous but Fig. 10 is a similar case which escaped detection by one of the keenest diagnosticians

of the knee and elbow. This seemed to open up the field of soft tissue radiography, and the lungs offered the most fertile field for its application.

During the winter of 1904–05 I made about one hundred radiograms of incipient or early cases of tuberculosis. Many of the patients were referred from the Vanderbilt clinic after a careful physi-

FIG. 9



signs. The physical examination was made and recorded by a very competent diagnostician, involvement of the right side. Radiographic findings: Diminished aëration of both apices, (Hickey's sign of tuberculosis); *D*, diaphragm retracted ; *F*, thickening around both roots; lobe, small area of consolidation; K^1, dilatation of the right descending bronchus filled process to reach the stage that is shown in the right lung without giving physical signs, in this city.

cal examination had been made and recorded by Dr. Austin Riggs and at least one or two other members of the medical staff. If they all agreed as to the physical signs, the case was only radiographed to

show the more advanced lesions; if they disagreed either on the character or location of the signs, the patients were radiographed and later the radiographic findings were compared with the physical signs.

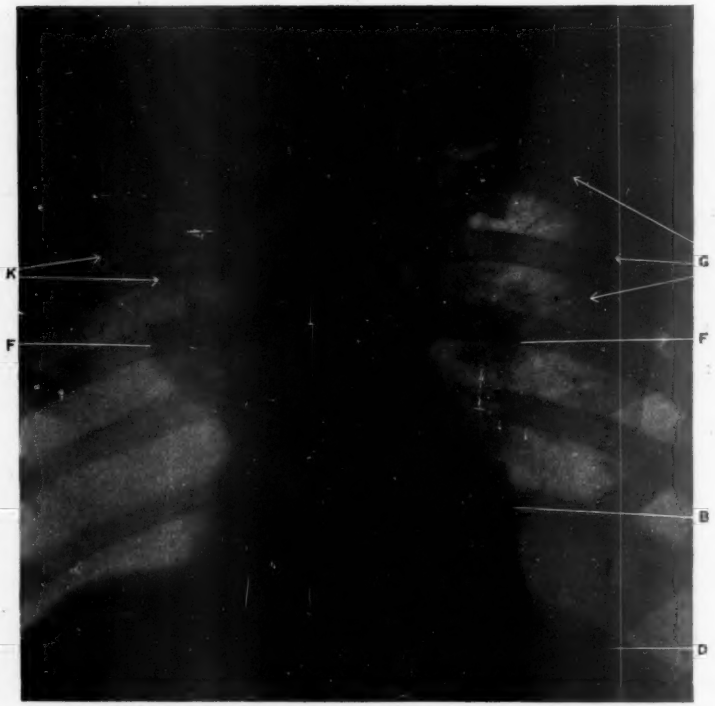


FIG. 10.—Illustrates how extensive a tuberculous process may exist without one of the keenest physical diagnosticians being able to detect it. A process had been detected at the right apex, and the patient was radiographed to determine whether there was a cavity. Physical signs of a cavity at the right apex. Equivocal signs above the clavicle on the left side, no physical signs below. Radiographic findings: Diminished aëration over both lobes, more marked on the right side; *B*, heart small; *D*, diaphragm normal; *F*, typical tuberculous infiltration around both roots; *G*, infiltration of the entire right lobe; *K*, ill-defined cavity at the right apex.

In every case in which the physical signs were present a well-defined lesion was found in the radiogram, and in many cases there were lesions in the opposite lung that gave no physical signs. This occurred in so many cases that I hesitated to make a diagnosis of tuberculosis, and decided to make radiograms of lungs post mortem.

Specimens were selected that had been removed from the thorax without tearing the pleura, they were drained of as much of the œdematous fluid as possible, inflated to about the extent of normal inspiration, and radiographed. These radiograms, one of which is shown in Fig. 1, showed just about the same detail that it is possible

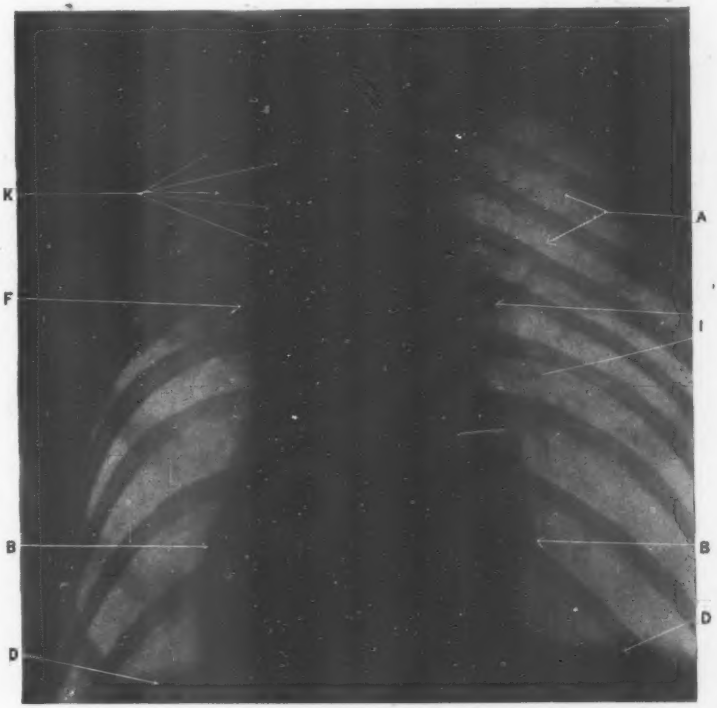


FIG. 11.—The history was typical of mixed infection with high temperature, sweats, cough, and expectoration; and physical signs of consolidation and cavity formation. This figure is to illustrate the necrotic type of infection. Posterior view: Diminished aëration at both apices, more marked on the left; *A*, normal markings; *B*, heart normal in size and shape and drawn somewhat into the vertical position; *D*, diaphragm normal; *F*, thickening around both roots, more marked on the left; *K*, multiple cavities without thickened walls and filled with exudate; *I*, calcified tubercles.

to obtain in a favorable living subject (Fig. 2), and shadows similar to those seen in the cases from the Vanderbilt clinic were found in all these lungs.

The specimens were then sectioned and compared with the radiograms; in most of the cases the lesions were readily found and identi-

fied as tuberculous. But some of the shadows, that resembled isolated tubercles scattered through the lung, were caused by one small bronchus or bloodvessel crossing the other, as seen on end section. One specimen of a child's lung appeared normal on external examination, but the radiogram showed several distinct old

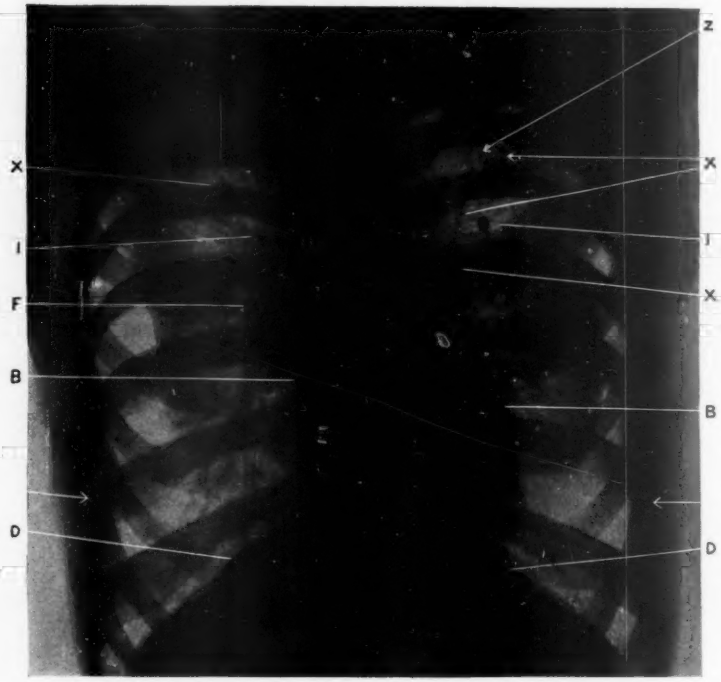


FIG. 12.—History of fifteen years of slight hacking cough, no expectoration, no tubercle bacilli in the sputum; slight physical signs; this is the most typical case of chronic miliary tuberculosis, involving the greater part of both lungs. Diminished aëration of both lungs. *B*, heart small and drawn into the vertical position; *D*, diaphragm arched up in the median line, thorax contracted; *F*, thickening around both roots; old calcified tubercles and fine mottled infiltration. Infiltration of both lungs, with extremely small, isolated (*X*) and conglomerate (*Z*) tubercles; *I*, calcified tubercles. The process shows no tendency to consolidation.

calcified lesions. On careful cross section these were not found, and the lungs were reported normal by the pathologist. Fortunately the sections were saved, and when these spots were localized by sticking hat pins in at different angles and making more radiograms, they were readily located; and when they were examined microscopically, they were reported as being tuberculous.

To the ultra scientific man this examination was unsatisfactory because the lungs had been removed from the thorax. I therefore tried to radiograph corpses at the morgue, just before autopsy, and other cases were radiographed immediately before and after death; but all these radiograms had the same appearance, and did not resemble the lung in the living subject as closely as did the inflated lung. It is largely on this series of radiograms of postmortem specimens that the interpretation of the accompanying plates is based.

Radiographically the following varieties of lesions may be recognized, but how accurately these coincide with the pathological classifications can only be proved by further pathological radiography.

CLASSIFICATION I.

- **Acute and subacute.**
  - **1. Exudative.**
    1. Isolated tubercules, large and soft (Fig. 3, *X*).
    2. Conglomerate tubercules (Fig. 3, *Z*, and Fig. 6, *Z*).
    3. Consolidation: large areas of consolidation surrounded by soft tubercles (Fig. 4, *H*).
  - **2. Productive.**
    1. Small isolated tubercles with clear-cut, well-defined edges (Fig. 7, *X*).
    2. Union of three or four tubercules to form a conglomerate tubercule (Fig. 7, *Z*).
    3. Small areas of consolidation (Fig. 7, *H*).
    4. Fibrous appearance extending from the root and connecting areas of consolidation (Fig. 7, *F*, *G*, and Fig. 9, *F*, *G*).
    5. Complete consolidation (Fig. 8, *H*).
  - **3. Necrotic Cavity.**
    - Single (Fig. 5, *K*).
    - Multiple (Fig. 11, *K*.)
    - Full of exudate (Fig. 11, *K*).
    - Empty (Fig. 5, *K*).
    - Without thickened walls (Fig. 11, *K*).
    - With thickened, calcified walls (Fig. 5, *K*).
- **Chronic.**
  - **Miliary.** Small, clear-cut, well-defined isolated tubercules involving the greater part of both lungs without consolidation (Fig. 12).
  - **Fibroid.** Fibrous consolidation with retraction of the ribs and diaphragm and displacement of the heart (Fig. 13).
  - **Calcareous.** Few, scattered, calcified tubercles at the right apex (Fig. 21, *I*). Group of calcified tubercles around the root causing hemoptysis (Fig. 20, *Z*).

The pure type of each of these varieties may readily be differentiated from one another, but when the exudative and productive processes are each present to about the same extent, it is difficult to state which is which. Necrosis may occur in either exudative or productive processes, and the calcareous deposits represent old healed lesions of either type. The acute or subacute exudative tuberculosis process is recognized radiographically in its early stage by large, soft, isolated tubercules (Fig. 3, *X*), the edges of which are not clear cut and well defined. It has a great tendency, even in the

early stage, to the formation of conglomerate tubercles (Fig. 3, *Z*) or small areas of consolidation. These go on rapidly to the typical form indicated by small areas of consolidation (Fig. 4, *H*) surrounded by large, soft, individual, or conglomerate tubercles. This variety of lesion may reach the stage of almost complete consolidation before the keenest ear detects the physical signs. Note the history under Fig. 3.

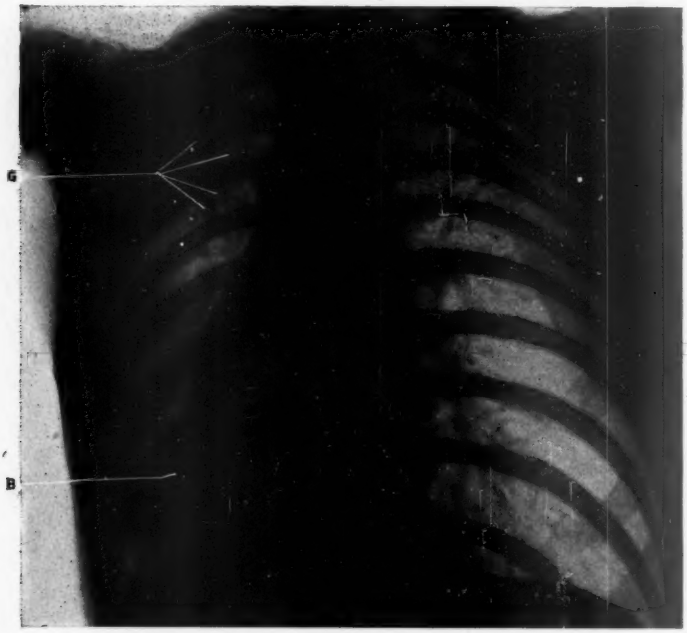


FIG. 13.—A case of chronic, fibroid tuberculosis, so-called fibroid phthisis. The left side of the chest is retracted. *B*, heart is drawn over to the left side, or some say pushed over by the compensatory emphysematous lung. In the upper lobe there is a typically mottled infiltration (*G*).

The subacute productive process is most typical in the early stage. The tubercles (Fig. 7, *X*) are small, dense, more isolated, and their edges are clear cut and well defined; and where several unite to form a conglomerate tubercle (Fig. 7, *Z*) they do not lose their identity. It does not go on rapidly to the stage of consolidation (Fig. 7, *H*), and the areas where it does occur are small and circumscribed; it can readily be traced back to the extension from the root by the fibrous appearance (Fig. 7, *FG*) that radiates from the root and connects the areas of consolidation.

The productive process may reach the stage of infiltration, or even consolidation (Fig. 8, *H*), or with cavities (Fig. 8, *K*), before physical signs develop, as is illustrated in Figs. 8, 9, and 10; in these cases the most careful physical examinations were made.

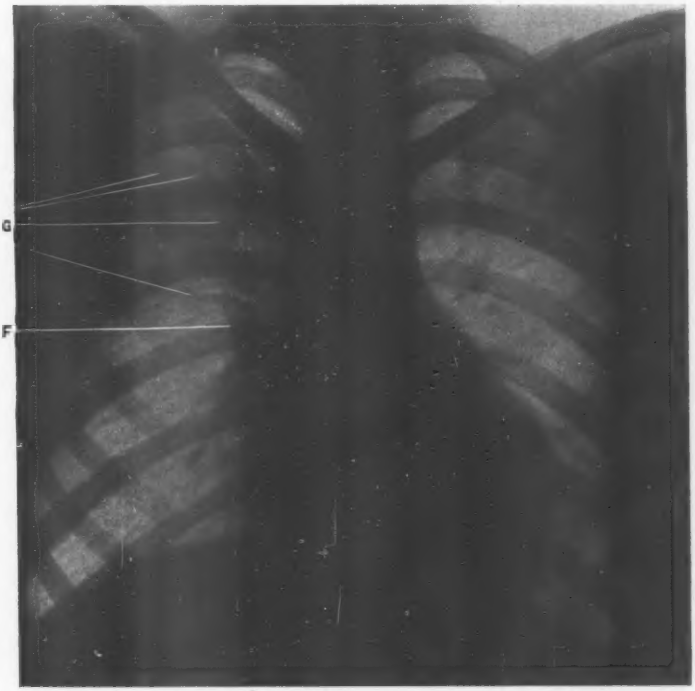


FIG. 14.—Illustrates the bronchial or peribronchial type of infiltration radiating from the roots of the lung. History equivocal. Physical signs: Few rales at the right apex, just below the clavicle, no dulness, or change of voice or breathing. Radiographic findings: Diminished aëration of both upper lobes, more marked on the right side; heart normal in size, shape, and position; diaphragm normal; *F*, typical thickening around the right root; *G*, radiating from both roots to the apices, more marked on the right side, are thickened bronchi without infiltration of the air cells supplied by them. This radiogram is especially interesting when compared with the following one (Fig. 15), where the process has extended and where there is an infiltration of the air cells.

Necrosis may occur in either the exudative or productive process, and the necrotic areas may be full of exudate and hard to differentiate (Fig. 11, *K*) from the surrounding consolidation, or they may be empty and the cavity show distinctly (Fig. 5, *K*). There may be multiple cavities (Fig. 11, *K*) in a consolidated area, with little or no attempt at walling off; or there may be a large cavity with a dense wall, probably infiltrated with calcareous deposits (Fig. 5, *K*).

Chronic miliary tuberculosis is recognized by the extremely small, clear-cut, well-defined tubercles (Fig. 12, *X* and *Z*). In the most typical case that I have seen both lungs were equally effected, the process showed no tendency to consolidation, and there was not the fibrous appearance usually presented in the chronic fibroid consolidation.

FIG 15.—This is one of the most classical plates of early tuberculous infiltration that I have made, but unfortunately is it very difficult to reproduce for publication. The original plate shows the following detail very distinctly: Diminished aëration of the left upper lobe; *B*, heart normal in size, shape, and position; *F*, thickening around both roots, more typically tuberculous where it extends out along the bronchus on the left side, having the appearance of the rough bark of a tree. The air cells supplied by this bronchus, and only these air cells, are infiltrated with miliary (*X*) and conglomerate (*Z*) tubercles giving the mottled appearance so typical of tuberculous infiltration of the lung (*G*). Family history: Father and mother died of tuberculosis. History: No cough, expectoration, or physical signs; loss of five pounds in weight and loss of sleep in the month of May, neither of which would ordinarily cause a patient to consult a physician for tuberculosis. The diagnosis of this case was made solely on the radiographic examination; the patient was treated accordingly, and the last I heard was perfectly well.

Chronic, fibroid consolidation is usually limited to one lung or part of one lung (Fig. 13). The consolidation may or may not be very dense and there is retraction of that side of the chest; frequently the ribs are drawn together, which gives a lateral curvature to the spine. The diaphragm is retracted and the heart is drawn to the affected side, or some say it is pushed over by the emphysematous lung on the opposite side.

Old calcified tubercles (Fig. 20, *I*) are most frequently seen at the root of the lung; they may be in the glands or in or around the walls of the bronchi, particularly the right descending bronchus and its branches (Fig. 17, *I*); they are usually the results of infection during childhood. When seen at the apex (Fig. 21, *I*) or at some other part of the lung, they are then the result of an old healed process probably of more recent origin, and are readily differentiated from the exudative or productive tubercule of an active or recently active lesion (Fig. 15, *X Z*).

Tuberculous infection may involve the lungs in the following ways:

CLASSIFICATION II.

Parenchymal involvement; may be exudative or productive, or a combination of both, and may have gone on to the stages of necrosis.	1. Limited to one or both apices (Fig. 3). 2. Limited to one lobe or the entire lung (Figs. 1 and 2). 3. Or it may involve part of both lungs (Figs. 8, 9, and 10).
Bronchial or peribronchial; may be exudative or productive, or both, but the productive process usually predominates.	1. Radiating in character from the root to the apex in adults (Fig. 1); to the base in children—old calcified (Fig. 17). 2. Bronchi alone may be involved (Fig. 14). 3. Bronchi and air cells supplied by bronchi may be involved (Fig. 15), with isolated (Fig. 15, *X*) or conglomerate tubercles (Fig. 15, *Z*). 4. Fibrous growth from the root without individual tubercles—not positively tuberculous (Fig. 14). 5. Bronchi may be normal in size with thickened walls, as in Fig. 15, *F G*; they may be dilated and filled with pus and exudate (Fig. 9, *K*), or empty—bronchiectasis (Fig. 9, *K*).
Root involvement may be glandular, bronchial, or peribronchial, either fibrous or calcareous.	1. Glandular may be circumscribed with clear cut edges (Fig. 16, *F*). 2. Groups of small glands connected by fibrous tissue which extends out along bronchi (Fig. 10, *F* and Fig. 17, *F*). 3. Bronchial or peribronchial thickening around the larger bronchi, without thickening of the root itself and without infiltration of the surrounding tissue (Fig. 18, *F*). 4. Or the walls of the larger bronchi may be thickened and seen on cross sections giving circles or the figure eight (Fig. 19, *F*). 5. This thickening may be shown in the active stage (Fig. 10, *F*), which is readily differentiated. 6. From the old calcified tubercules of a healed lesion (Fig. 20, *I*). Root (Fig. 20). Branch of descending bronchi (Fig. 17, *I*). Apex (Fig. 21).
Tuberculosis may be differentiated from	Dry pleurisy. Pleurisy with effusion. Empyema. Carcinoma. Aneurism.

The exudative, productive, or combination of both processes may involve the parenchyma of the lungs, and it may go on to the

stage of necrosis. It may be limited to one or both apices (Fig. 3), or one lobe (Figs. 5 and 6), or it may involve one entire lung (Fig. 13), or part of both (Figs. 8 and 9).

I have never seen a tuberculous lesion of the parenchyma without a typical tuberculous infiltration around the root. In some cases it is difficult to show the connection between the two processes, but with improved technique and more pathological radiography I think that it will be established that all tuberculous lesions begin at the root and extend to the parenchyma.

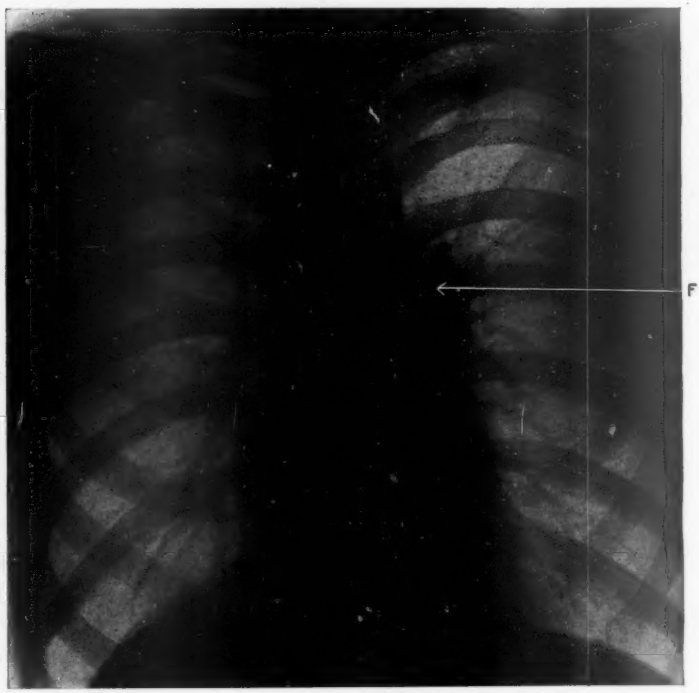


FIG. 10.—Shows a circumscribed gland (*F*) on the left side, opposite the tip of the third rib.

Radiographic examination of incipient cases indicates that in a very large percentage of cases the lesion at the root is more extensive than the parenchymal lesion; and so frequently radiograms show a distinct lesion at the root with no parenchymal involvment that it is reasonable to assume that it extends from the root to the parenchyma. Radiating from the root to the apex in adults (Fig. 14), and to the base in children, may be seen infiltration in and around the walls of the bronchi, giving the appearance of the rough bark on the

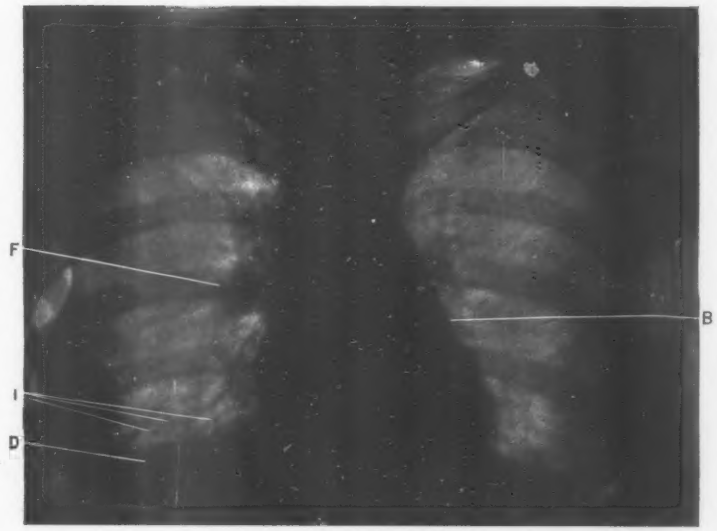


FIG. 17.—Illustrates typical acute infiltration around the root and old calcified tubercules (*I*) around the right descending bronchus, with localized retraction of the diaphragm (*D*); *B*, heart normal; *F*, acute infiltration around the root; *D*, diaphragm, localized retraction in the area of old calcified tubercles (*I*)

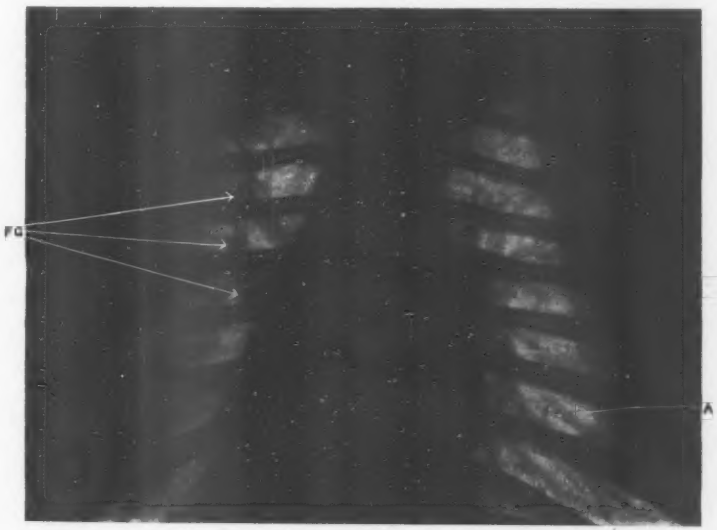


FIG. 18.—Illustrates infiltration around medium size bronchi like a fan, without infiltration around the root. Posterior view: *A*, normal markings of the lungs show distinctly; *FG*, bronchial or peribronchial infiltration of medium size bronchi spreading out like a fan.

branches of a tree (Fig. 15, *F*, *G*); the air cells supplied by these bronchi are infiltrated with isolated (Fig. 15, *X*) or conglomerate (Fig. 15, *Z*) tubercles. The process has the appearance of a tree budding in the springtime. There may be a diffuse fibrous growth extending from the root, without individual or conglomerate tubercles, giving the appearance of a general fibrous thickening and lack of aëration (Fig. 14, *G*). I am very cautious about making a diagnosis of tuberculosis in those cases in which the typical tubercles are absent. The bronchi may be normal in size (Fig. 15, *F*, *G*),

FIG. 19.—The only symptom was hemoptysis. The physical signs were absolutely negative. This was a test case examined for admission to the Saranac Sanatorium, and there were absolutely no physical signs of tuberculous infection. Repeated radiographic examinations showed a typical figure-of-8 thickening (*F*) around the root, surrounded by scattered tubercles (*X*). The patient was sent to Saranac solely on the radiographic findings; reacted to tuberculin injections, and later developed physical signs over this area, but recovered rapidly.

or they may be dilated and full of exudate (Fig. 9, *K*), or empty (Fig. 9, *K*). Tuberculous infection around the root of the lung may involve the glands (Fig. 16), the bronchi, or it may be peribronchial in character.

Glandular enlargement may be circumscribed with clear-cut edges (Fig. 16, *F*), but more frequently there is a group of small glands connected by fibrous tissue which extends out along the bronchi and bloodvessels (Figs. 10, *F*, and 17, *F*). There may be infiltration in or around the larger bronchi without thickening at the root and without parenchymal involvement (Fig. 18, *FG*)

The walls of the larger bronchi may be infiltrated, and when seen on cross section give the appearance of circles or figure "8" (Fig. 19, *F*), and may be surrounded by a few isolated tubercules (Fig. 19, *X*), which would indicate activity. The infiltration of the root may be shown in the active stage (Fig. 10, *F*), when it has a soft

FIG. 20.—This radiogram illustrates a group of calcified tubercles in the walls of the large bronchi, causing hemorrhage on exertion. History: During or immediately after a game of basket-ball this girl, who had previously been perfectly healthy, had profuse hemoptysis without other symptoms, and with absolutely no physical signs to indicate a tuberculous process. The girl consulted a physician who has all doubtful cases of the chest radiographed, regardless of whether he gets physical signs of tuberculous infection or not. A series of these plates showed a group of calcified tubercles around the root of the right lung, in close proximity with the base of the heart, and I believe that, either from forced heart or respiratory action, these tubercles scratched through the membrane, and caused profuse hemoptysis. The physician who referred the patient to me made a positive diagnosis of tuberculosis, based entirely on the radiographic findings. The attending physician, in another vicinity, ridiculed the diagnosis, because of the absence of physical signs. Several months later physical signs developed and the diagnosis was confirmed. The girl went to Colorado, and the process was checked. This is only one of several cases in which there was hemoptysis on exertion, with no physical signs. Swimming and basket-ball are the exercises that have caused the hemoptysis in most of these cases.

diffuse appearance, which is readily differentiated from the old healed calcified lesion (Fig. 20, *I*), which is usually the result of infection during childhood.

Healed tuberculous processes vary in their appearance according to the variety and extent of the lesions and the time that has elapsed since they were active. The exudative process when checked shows a much greater tendency to resolve than is generally supposed, and

all that may remain of quite an extensive exudative process is a few scattered calcified tubercules (Fig. 21, *I*).

The productive process tends to a fibrous thickening that sometimes seems to resolve or at least diminish in density. This is

FIG. 21.—This illustrates a normal chest except a group of old calcified tubercles at the right apex, which are all that remain of quite an extensive process that was active nineteen years previously. No physical signs were apparent. Normal markings of the lungs show distinctly. *B*, heart normal in size, shape, and position, diaphragm normal; *F*, thickening around the root (old process); *M*, mammary gland should not be mistaken for consolidation; *L*, calcified costal cartilages should not be mistaken for calcified tubercles; *I*, old calcified tubercles at right apex.

probably a mixed process; and the exudate resolves and the fibrous process contracts. The old calcified lesions are found most frequently around the root (Fig. 20, *I*) and the right descending bronchus

(Fig. 17, *I*), and are the result of infection during childhood. These are present in a very large percentage of cases, thus corroborating the cutaneous reaction made by von Pirquet, referred to early in this paper.

The differentiation of tuberculosis from other pulmonary lesions may be definitely made solely by the radiographic examination. Dry thickened pleura may be differentiated from tuberculous infiltration by the smooth, homogeneous appearance and the normal markings of the lung showing through. Pleurisy with effusion has a smooth, homogeneous appearance shading off gradually to the density of the lung at the upper surface of the fluid. Empyema, especially if encapsulation, is of equal density throughout, with clear-cut edges, and it does not have the mottled appearance of tuberculous infection. Carcinoma has an appearance similar to the fibrous consolidation, but it has more of a nodular appearance, and unless complicated by tuberculosis no individual or conglomerate tubercles are present. Aneurysm has to be differentiated only from mediastinal glandular involvement, and this is sometimes difficult unless a fluoroscopic examination is made to see whether the tumor pulsates.

Considering the large percentage of cases in which tuberculosis is found at autopsy when only a few gross sections are made of the specimen, and the fact that the Germans say that 98 per cent. of all adults have or have had a tuberculous lesion of the lung, and that 93 per cent. of children reacted to the cutaneous tuberculin test, it is not a question of who has tuberculosis, but what is the variety and extent of the lesion and is it active or inactive.

If pulmonary tuberculosis can be diagnosticated radiographically as early and accurately as now appears, and if one can state with a reasonable degree of certainty the variety of the lesion and whether it is active or inactive, and can determine with absolute certainty whether the process is advancing, held in check, or resolving, it seems that the question of the diagnosis of incipient pulmonary tuberculosis is solved.

THE MEDICAL ASPECTS OF THOSE TOXEMIAS OF PREGNANCY WHICH TEND TOWARD ECLAMPSIA.

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In the process of childbearing certain physiological activities are inaugurated which, when successfully completed, introduce into the world an independent being. Some women are never so well as during, and for a time following, pregnancy; in others, anatomical

and functional aberrations arise which may be characterized as slight, moderate, or severe; in yet others, happily few, the results are abortive and destructive. With a physiology stimulated to beneficent constructive activity, on the one hand, and perverted to the most pronounced pathology, on the other, the investigator may well seek for the heretofore elusive essential causative element. The physiological features interest us as scientists; the pathological problems deeply concern us as physicians. Perhaps future discoverers, advancing beyond the realms of speculation, may demonstrate that, as the result of incomplete or inharmonious complemental union of the attracting centrosomes of the spermatozoön and ovum, some substance is developed, increased, and intensified by subsequent fœtal growth, which, entering the maternal circulation through the syncytium, is deleterious to the gravid woman, and is the primary cause of the toxemias of pregnancy. Without attempting to review the facts upon which the opinion is predicated, we may, for the present, safely assume that the primary offending material is elaborated within the fœtus and its adnexa; that it is specific in character; that it is responsible for certain maternal lesions and disorders, as hepatic, renal, and others; and that secondary toxins consequent upon such pathology play important roles in the late toxemias which lead toward eclampsia.

Shortly after impregnation, at a period probably coincident with the establishment of maternal and fœtal circulatory connection, certain special symptons arise. Of these, the peculiar vomiting of pregnancy is the most striking. Ordinarily it is of such character and degree that it gives rise to no apprehension upon the part of either patient or physician. In the comparatively rare cases, however, it attains the dignity of hyperemesis—the so-called pernicious vomiting of pregnancy—and may become an element of great danger. In such cases the symptoms are unlike those of any other morbid condition, and the anatomical changes are quite special. The distressing features of the nausea and vomiting need not be depicted; the ejected aqueous liquid, mixed with mucus and bile, is notably ammoniacal and acrid. The scanty urine is dark, and heavy with solids; the well-maintained total nitrogen output includes a notable, or even a remarkably large, proportion of ammonia; possibly acetone and diacetic acid may be present; only as the danger line is passed do albumin and casts appear. In desperate cases hemorrhages may occur, with marked pallor; the blood pressure declines, prostration is profound, and hebetude supervenes; there may be slight, but very rarely is there deep, jaundice, although there is almost always tenderness over the liver. Post mortem there is found, distinctively, necrosis of the central portions of the hepatic lobules, with consecutive cellular degenerations. The kidneys are large, soft, and pale, with slight tubular and possibly other parenchymatous alterations. The condition manifests itself during the third and fourth months, appearing only rarely at a later period of pregnancy.

It may be well at this time to consider cursorily certain subjects which are of more or less importance in the process of childbearing: Thus, there is pituitary hyperplasia during pregnancy, but it is probable that the special secretion of this gland is required in uterine development, and in its final great physiological feat. It is a matter of common observation that thyroid activity is stimulated by menstruation and pregnancy, and it has been alleged that the markedly athyroidic subject is especially liable to the late toxemia which tends toward eclampsia. In such conditions benefit may be noticeable after the adminstration of thyroid extract, but this may be due to the induced lowering of the blood tension, and not to any specific action. Removal of the parathyroids is often followed by tetany, and certain animal experiments appear to show that parathyroid feeding may prevent eclampsia, but further evidence is required before any great importance is attached to these studies. The connection between adrenal hyperplasia and the increase in blood pressure and impending and present eclampsia has not been worked out.

In the toxemic state preceding eclampsia there may be found, often if not regularly, cerebral œdema, with high tension of the cerebrospinal liquid. If convulsions have occurred, there are, usually, numerous minute extravasations of blood scattered throughout the brain, with large hemorrhages into the ventricles.

Mention has been made of the hepatic lesions found in connection with, and apparently characteristic of, the pernicious vomiting of pregnancy. In the later toxemias the liver presents anatomical changes equally distinctive. Essentially these consist of hemorrhages in and about the portal spaces, cloudy swelling, fatty degeneration, and necrosis of the hepatic cells. In some instances the microscopic findings are such as to lead to the plausible conclusion that the liver of earlier pregnancy had been carried along to the eclamptic period, with the hemorrhages as a terminal addition. Macroscopically there may be more or less extensive hemorrhages beneath the capsule and throughout the organ. During life the liver is tender and demonstrably enlarged. Slight icterus may be noticeable; profound jaundice is very rare. Acute yellow atrophy of the liver is encountered very much more frequently in pregnant women than under any other circumstance, but the large incidence is clearly due to the inviting field presented, and not to a specific cause connected with the gravid state. It has been assumed, in some quarters, that there is a special "liver of pregnancy," characterized by a definite insufficiency, manifesting itself most noticeably by the incomplete conversion of ammonia into urea, but if this is true the demonstration must be difficult.

In practically all cases of eclampsia there are renal changes which appear identical with those of acute nephritis. The kidneys are large, pale, and of diminished consistency. Microscopically the alterations are found almost exclusively in the cortical convoluted

tubules, with slight glomerular involvement. Rarely are more extensive changes observed, unless the patient is also the subject of a chronic nephritis. Prompt anatomical recovery is the rule. This condition, known as the "kidney of pregnancy," often develops rapidly, and is accompanied by scanty and albuminous urine, casts, etc.; occasionally anuria supervenes.

The urinary excretion in pregnancy has been the subject of elaborate and painstaking investigation, as well merited by its importance, for it is here that the first resonant note of alarm is sounded. It is true that to the attentive observer there will be disclosed other and earlier indications of the gathering storm, yet by common consent, and with good and sufficient reasons, the appearance of albumin in this liquid has been long considered the line beyond which security does not dwell. The simple fact of its presence is sufficient evidence of the proximity of danger; the manner of its advent is dramatic. General acceptance will probably be given to the statement that, as a rule, the urine of the gravid woman is, compared with that of health, lighter in color, diminished in specific gravity, deficient in chlorides and urea, while the sulphates are increased, possibly with the appearance of indican. To this rule there are exceptions, the output of urea and salts being well maintained or exceeding the normal, but I must confess that, within the limits of my observation, these have not been as reassuring as might be inferred; indeed, to me a dark and markedly acid urine, rich in urea and other solids, is a disturbing circumstance, leading to concern or anxiety. It is probable that reduplication of my own experience is responsible for the widespread mild distrust within the medical profession as to the value of frequent and careful examinations of the urine in these cases. Nevertheless, a moment's consideration of the subject should disclose the weakness of such a position. Granting that albuminuria sometimes suddenly makes its appearance in cases showing no previous deviations from the urine of normal pregnancy, or of health, the significance of its advent is not diminished in the least; acute nephritis, the "kidney of pregnancy," and a grave toxemia are present.

Œdema has long been observed in connection with the albuminuria and eclampsia of pregnancy. Manifest œdema is obtrusively prominent, and is easily recognized; but this is preceded by an overful state of the intercellular tissue-lymph spaces, a condition which may be called occult œdema. In this variety the normal laxity of the soft tissues gives place to increased resistance; there is a notable sense of exalted tension, which is subjectively perceptible to the patient and objectively detectable by the examiner; the blood pressure is raised, sometimes to a great height; the eyes are prominent, and the face, trunk, and extremities are noticeably plump; there is no pitting upon pressure, because the resiliency of the areolar tissues is maintained; manifest œdema is imminent. In this condition there is

advancing grave disturbance of the delicate balance existing between the vascular, lymphatic, and extravascular tissue-lymph circulation, and with this probably begins the danger period for the gravid woman. To the burden of the incoming fœtal toxins there is now added the accumulating toxic cellular waste of the pregnant woman herself. So far as the imminency and extent of the risks of eclampsia are concerned, there is probably little choice between occult and manifest œdema; there is a larger accumulation of deleterious matters in the latter, but the system is partly protected by the short-circuiting of the extravascular circulation.

If there is any blending of the toxemia of gravidity and uremia in the genesis of eclampsia, here is the ground upon which they must meet. There may now appear upon the scene high blood pressure, tinnitus, amblyopia, muscular twitchings, etc., followed by convulsions or coma, all of which are prominent symptoms of uremia. However, should death occur, there is this notable anatomical difference, namely, that whereas hepatic, pulmonary, and, especially, massive cerebral hemorrhages are uncommon in simple uremic convulsions, they are the rule in eclampsia. Nevertheless, after a careful review of this question, I am, tentatively at least, of the opinion that in such cases there is added to the primary toxemia of pregnancy a secondary uremia, although I am not prepared to urge strongly its acceptance upon others.

For many years I have been deeply interested in the behavior of the extravascular circulation, and the composition of the tissue lymph in cases of occult and manifest œdema. In these cases there is lymphatic insufficiency; tissue-lymph circulation is impeded or short-circuited; nutritive material fails to reach freely the various cells of the body; waste products of cellular metabolism are not adequately discharged; effete and toxic substances accumulate in this liquid. Remedially, considerable or large quantities of this tissue lymph, heavily laden with cellular debris, deleterious toxins, and saline accumulations, may be readily removed (measured and analyzed), and with evident symptomatic and fundamental benefit to the patient. I am of the opinion that the usefulness of this procedure may be enhanced by early recourse to it, at a time, indeed, which will materially anticipate eclamptic imminence.

That prominence may be lent to some of the pratical points above mentioned the pertinent details of an illustrative case are given:

A lady, of general good health, aged thirty-four years, who had had scarlet fever at thirteen years, and gave successful birth to a child, after a short period of albuminuria and threatened eclampsia, at twenty-eight years, entered upon a second pregnancy early in December. At the end of the first month she was in excellent condition; the eye grounds were normal; there were no evidences of cardiac insufficiency; the systolic blood pressure was 130 mm. Hg.; the urine was normal in quantity and character; there was moderate

nausea and vomiting. The vomiting ceased in the fourth month; the blood pressure remained unaltered; the urinary findings were practically unchanged, with the exception that the sulphates gradually increased in amount, and indican appeared at the end of the third month. At the end of the sixth month a few hyaline casts were detected in the urine. One week later there was an abundant albuminuria. The blood pressure quickly rose from 135 to 160. Occult œdema was present. During the following week the average daily excretion of urine was 1600 c.c., with an intake of about 2000 c.c. of liquids. The urea output ranged between 43 and 17 grams per day. The chlorides were about normal, but the phosphates and sulphates were reduced. The albumin varied from 4 per cent. to 17 per cent. Only rarely were a few hyaline casts found. There were flashes of light before the eyes, amblyopia, headache, sleeplessness, restlessness, nystagmus, general nervous tension, muscular twitchings, etc. Fœtal movements, if present, were slight and not objectively noticeable. During the next three days the blood pressure rose to 185; the urea excretion varied from 15.4 to 18 grams daily; the chlorides rose to volumetric percentages of 37 to 45; the phosphates and, especially, the sulphates were reduced; albumin was present to from 27 per cent. to 38.5 per cent. by volume; hyaline, granular, and blood casts were abundant. During these three days there was drained away more than 6500 c.c. of intestinal serum, having a specific gravity of from 1012 to 1018, acidity of 10°, urea to 0.2 per cent., chlorides to 18 per cent., and sulphates to 10 per cent. by volume. During the following three days the urine continued scanty, with urea from 14 to 19 grams per day; the chlorides rose to the great height of 62 per cent. by volume; albumin was present to 42 per cent., 39 per cent., and 20 per cent. on the respective days; casts were found in rapidly diminishing numbers; the blood pressure declined to 142; the sleeplessness, restlessness, nervous tension, muscular twitching, and other symptoms of eclamptic imminence subsided. During the following week the urine gradually approached the normal in character, with a reduction of the albumin to traces, and the casts to occasional findings; the blood pressure fell to 132, which is about normal for this patient. At the end of this period a shrunken seven months' child was born, apparently having been dead for several days. Recovery was prompt and complete. The management included confinement to bed; bleeding to 600 c.c.; sweating; reduction of the food to liquids little more nutritious than water; the evacuation of serum, via the intestines, to the extent mentioned, by the use of elaterin, adminstered in the manner advocated in another publication.[1]

It will have been noticed that studied care has been exercised in avoiding any reference to those large and important obstetrical problems which are involved in the management of those toxemias of

[1] Jour. Amer. Med. Assoc., 1909, liii, 1796.

pregnancy which tend toward eclampsia. Upon these I have no views to express, but it should not be assumed that, in presenting some of the medical aspects of these conditions, I am insensible to the primary lesson to be learned from a proper consideration of the fact that evacuation of the uterus upon the earliest appearance of danger will promptly save almost all these women, with, probably, but little difference in the child mortality. Neither should it be inferred that, in calling attention to a method of ridding these patients of a portion of the toxic load under which they may be staggering, I am advocating it as a measure to be substituted for forcible delivery. My object will have been attained if the subject has been presented in such manner as to indicate clearly that the primary specific toxic agent is of fœtal origin, and probably attacks the pregnant woman by way of the placenta; that certain distinctive anatomical changes are induced in the liver and kidneys; that these are followed by tissue-lymph circulatory insufficiency, with consequent accumulation of toxic substances in this liquid, occult or manifest œdema, and eclamptic imminency; that by draining off a portion of the excess of tissue lymph, heavily laden with deleterious and dangerous toxic substances, cellular nutrition may be promoted, many of the prominent symptoms of eclamptic imminency relieved, and the patient benefited.

DISTURBANCES OF THE THYROID SECRETION IN NORTHERN MEXICO.

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We need a short comprehensive term for a number of interesting conditions ranging between the extremes of myxœdema and exophthalmic goitre. Levy, Rothschild, and Huchard have entitled a recent paper "Thyroid Instability."[1] This is short enough, but seems to refer more to a functional trouble, whereas the symptoms are generally caused by definite progressive changes in the gland.

There are towns in the mountainous state of Sonora where goitre is endemic, and it would seem that northern Mexico is a splendid field for the study of these disorders. A large proportion of the women have enlarged thyroids, and cases of moderate thyroidism are seen constantly.

Haller, in 1730, quoted the suggestion of Ruysch that the "blood-vessel glands" elaborate some substance that is thrown into the

[1] Bull. de l'Académie de méd., May 18, 1909.

blood current. A hundred years later, Bernard gave us the term "internal secretion," and since then a host of able experimenters have been at work in this field. Although cretinism and myxœdema are now easily cured, especially in the early stages, there is some cause for disappointment when we consider that, in the absence of an especially skilful surgeon, the physician today can do little more for a patient with exophthalmic goitre, the commonest and severest of these disorders, than he could in the time of Parry, Graves, and Basedow.

Although we are now recognizing certain symptom-complexes as of thyroid origin, we have much to learn as to the direct causation of the separate symptoms. Many of them are plainly due to the accelerated or retarded metabolism, as the case may be, and in hypothyroidism, malnutrition of the nervous system, muscles, and skin is a prominent factor. Some of the symptoms of thyroidism are those of angioparalysis, and angiospasm may be present in the opposite disorder. It is also entirely probable that the thyroid secretion is composed of various elements, and that some may be diminished or absent, while others are normal or overactive. This can help us to understand those puzzling cases in which symptoms of hypothyroidism and hyperthyroidism are plainly present at the same time. Pitfield[2] suggests that the thyroid secretion may be almost as complicated as the blood plasma, with its different functions. Another explanation offered in these cases is that an organ functionating defectively is liable to go to the opposite extreme in the effort to restore its balance.

Myxœdema, exophthalmic goitre, and cretinism have been recognized for many years, but of late our attention has been drawn perhaps more to the incomplete forms—"formes frustes" of the French. With the better understanding of these disorders, we will be able properly to classify many cases of so-called neurasthenia, hysteria, rheumatism, etc., and we will more often recognize an inefficient thyroid as a complicating factor in obscure cases. Frequently now the diagnosis has to be proved by the marked relief obtained from thyroid medication. And even this is not conclusive evidence, as shown by the articles that have appeared, claiming thyroid as a cure for most of the ills to which flesh is heir. If its usefulness in some unrelated disorders be confirmed by time and experience, further channels of research will be opened up.

Thyroid affections occur much more frequently in women than in men—thyroidism in the young, and hypothyroidism in the middle-aged. The trouble often seems to date from some infection such as grippe. Incomplete myxœdema appears generally about the time of the menopause, and often seems to cause the annoying symptoms of that epoch. According to Nichols, the disease

[2] Amer. Jour. Med Sci., 1907, cxxxiv, 859.

delays the menopause, but in many cases it seems to cause first a tendency to severe uterine hemorrhages, and then an early climacteric.[3] Pitfield believes it to be one of the penalties of childbearing, but it does occur in the unmarried and the nulliparous, and we need more statistics on the subject.

The relation between the thyroid and the reproductive organs, especially of women, has been known since ancient times. The gland often enlarges at puberty and during menstruation and pregnancy; the genitals do not develop in cretinism; pregnancy may cause temporary disappearance of myxœdema, etc. The term "paroxysmal hypothyroidism" has been applied to a condition in which the harsh and uncontrollable voice, and other symptoms of incomplete myxœdema recur with each menstrual period. Cases illustrative of these facts can be found in recent articles by Elliot[4] and Pinard.[5]

One of the most prominent symptoms of all these disorders is asthenia, which causes a giving way of the knees quite characteristic of hypothroidism. Osler's text-book mentions it as a symptom of Graves' disease. It is probably due to the weakness alone and is commonly experienced by athletes after an exhausting race. The weakness would be bad enough, but these patients generally take on flesh, which greatly adds to their discomfort. It would seem sometimes that the improvement noted in a given case could be due simply to the loss of weight caused by the thyroid medication. The increase in weight is one of the results of the sluggish metabolism, which, in its turn, is due to a lack of the accelerator effect of the thyroid secretion. The constant chilliness and coldness of these patients may be due to the same cause and to the anemia and dryness of the skin. One of the characteristic features is the presence of triangular pads of fat over the clavicles. The left one is often hyperesthetic.

The characteristic facial expression has been described as one of sorrowful fatigue. The intelligence may be slightly impaired, and there are hallucinations, especially of hearing. Tinnitus aurium is common. One of the most constant complaints is of anginoid pain under the left breast. This may possibly bear some relation to the heart changes which are generally present. Headache and backache are common, as are rheumatoid pains in all the larger joints. It is interesting to note here that marked changes are found in the epiphyses of the long bones of cats after thyroidectomy,[6] and that there is a retardation of the calcification of the cartilages in cretins, as shown by the x-rays.[7] It is not impossible that similar

[3] Jour. Amer. Med. Assoc., 1909, lii, 1162.
[4] Amer. Jour. Med. Sci., 1907, cxxxiv, 390.
[5] Ann. de gyn. et d'obstét, May, 1909, 257.
[6] Mit. aus d. Grenzgeb. der Med. u. Chir., 1907, xviii, 329.
[7] Amer. Jour. Med Sci., 1909, cxxxvii, 496.

changes occur in hypothyroidism, and that poorly nourished and painful epiphyses simulate rheumatic joints.

The skin occasionally has an olive tint, and it is almost always dry and scaly. The hair is often prematurely gray, and on account of the dryness and brittleness it soon becomes scanty on the eyebrows, axillæ, and back of the neck. Sweating, when present, may be localized to some one part of the body. Transitory œdema may be seen on the face and extremities, hence the frequent diagnosis of nephritis in these cases.

The heart is often somewhat dilated, and there are murmurs, due probably, in most cases, to relative cardiac insufficiency. As a rule, the dyspnœa present is out of all proportion to the heart findings. The pulse is rarely over 100, and the blood pressure is liable to be high. The teeth are generally carious. The buccal mucous membrane is often swollen so as to show marks of the teeth.

The thyroid may be too small to be palpated, or there may be a larger goitre. The symptoms depend not on the size of the gland, but on the amount of damage done to the secreting parenchyma. The voice often becomes harsh, and the patient loses control over it. It is interesting to note here that Pineles[8] has observed these spasms of the larynx after operative injury to the parathyroids. The blood generally shows some anemia and a lymphocytosis. There is some poikilocytosis, and in severe cases there are normoblasts. The lymphocytosis is found also in thyroidism. Transient albuminuria is common.

The following history is that of a fairly typical case of incomplete myxœdema:

Case I.—Mrs. O., Mexican; widow; washerwoman; aged forty years; complains of anginoid pains under the left breast, and dyspnœa on exertion. She was healthy as a child. Menstruation began at fifteen, and was scanty, lasting three days. Married at nineteen, she has had three healthy children, the last nine years ago. There never was any hemorrhagic tendency.

The present complaint dates back four years to an attack of bronchitis. The cough soon disappeared, but she has been growing so weak that she can get up a hill only with difficulty, and has had to restrict her work to ironing. Her knees will often give way from under her on the street, causing her great embarrassment. There have occasionally been tremor of the hands, and nocturnal attacks resembling asthma. She is quite intelligent, and her memory has remained good. There are hallucinations of hearing and tinnitus aurium. Besides the pain in the left side, which annoys her most, she often has severe temporal and occipital headaches, rheumatoid pains in all the larger joints, and obstinate backache.

[8] Wien. klin. Woch. April 30, 1908, xxi, 641.

She has become stouter in later years. She always feels cold, and sometimes an entire limb feels numb and frozen. There is formication over the left breast. The skin has been dry and scaly several years; she became gray at thirty, and the hair is brittle and falls out easily. The eyelids are sometimes puffy. There has never been any œdema of the legs. Appetite and digestion are good, and there is no constipation. Since girlhood her voice has become harsh and unruly during menstrual periods, and it is that way most of the time now. For the last seven years menstruation has been more profuse, lasting eight days, and occasionally occurring twice in the month.

The patient is short and stout, and looks prematurely gray. The buccal mucous membrane is œdematous and plainly shows the prints of the teeth on tongue and cheek. The circumvallate papillæ are greatly hypertrophied. The uvula is œdematous. Hearing is good. The thyroid gland is palpable but very small. There are two large triangular pads over the clavicles. The left one is the more prominent, and is painful and sensitive on pressure. The lungs are normal. The heart shows slight enlargement to the left, and there is a murmur indicating some incompetence of the mitral valve. The pulse is regular and 60 per minute. The palpable arteries are in good condition. The deep reflexes are slightly exaggerated, but the abdominal, epigastric, and plantar cannot be elicited. Sensation is not impaired, and the musculature is good. The fingers are short and thick, resembling those of advanced myxœdema. The urine contains neither albumin nor sugar. The blood is quite normal except for 70 per cent. of hemoglobin and a moderate poikilocytosis. The polynuclears are 64 per cent.; the lymphocytes, 22 per cent.; the large mononuclears, 14 per cent.; no eosinophiles were seen.

Fifty two-grain capsules of desiccated thyroid gave complete relief from all the symptoms in a month. She had lost weight, was brighter, the pains and asthenia were gone, and the heart murmur disappeared. The right fat-pad disappeared, and the left was much less noticeable. During the next few months she took a few more capsules, and over a year has now passed without recurrence of symptoms.

The interesting features of this case are: The paroxysmal hypothyroidea, which she has had throughout her sexual life; grayness at the age of thirty; tremor, which is more a symptom of thyroidism; slow pulse; and the hypertrophy of the circumvallate papillæ, which is possibly of some significance when we remember the close embryological relation of the base of the tongue and the middle lobe of the thyroid. I have noticed in several cases that the skin reflexes are absent, while the deep reflexes are normal. With sensation practically unimpaired, it is still possible that the reflex path is blocked in the abnormal skin. This is a point of some interest, and perhaps

diagnostic import. Many of the reports consulted in regard to this particular do not mention the reflexes at all. Howard[9] says that the superficial reflexes are sometimes diminished and rarely absent. Many things have been rare only until attention was directed to them.

The next case is very unfortunately incomplete, as the patient left before the symptoms of hypophyseal involvement could be thoroughly studied.

Case II.—A. R., Mexican; a cook; aged thirty-five years; a widow, complains of pain radiating from her feet to her hips. She enjoyed fair health up to a month ago, when she had la grippe. Menstruation was regular and uneventful until it stopped at the age of twenty-nine. A year later she began to get gray. She was married only seven months, and never conceived. Her voice has lately become coarse and harsh, and is all the more noticeable to her, as she used to sing with a good soprano before. She has been unable to do much work for the last two weeks on account of pain in the legs. She gets out of breath and has a coughing fit on climbing a hill. There is no cough at other times. Her knees give way when she is tired. Her memory is very bad, and she has hallucinations of hearing. At times she has been very deaf. Some time ago she was bothered by an unnatural somnolence, and has even gone to sleep standing up. Her hair has fallen out a great deal, and it has entirely disappeared in the axillæ. The skin is dry and rough, and the feet seem to do the sweating for most of the body. She is always cold. She often has pain in the left axilla.

The patient is a short, heavy woman, with a peculiar olive tint, which she says has been deepening since the menopause. Her hair is well streaked with gray. The face is slightly paretic on the right side. Eye movements are normal and the pupillary reflexes are intact. There is no icterus of the scleræ, and the lids are not œdematous. The tongue is extruded markedly to the left, and can be brought to the median line only with effort. The thyroid is very small. There are typical pads over the clavicles, and the left one is painful. There is a ring of fatty tissue about the lower ribs. The lungs and heart are apparently normal; the pulse is regular, full, and strong, 80 to the minute. The arterial walls are good. The liver is slightly enlarged. The fingers are well shaped. Many of the joints crack loudly when moved. There is slight œdema of the legs. The plantar arches are weakened, and flatten out under her weight. The deep reflexes are slightly exaggerated, but the skin reflexes cannot be elicited. The musculature is good.

There is 85 per cent. of hemoglobin; the leukocytes are normal in number; polynuclears, 47 per cent.; the lymphocytes, 33 per cent.; the large mononuclears, 18 per cent.; and eosinophiles, 2

[9] Jour. Amer. Med. Assoc., 1907, xlviii, 1404.

per cent. There are many microcytes and macrocytes, but no normoblasts.

The arches were immediately supported, better shoes secured, and the pains in the legs lessened. Six grains of thyroid a day soon caused marked thyroidism, and the dosage had to be reduced by half. The flat feet probably caused the pains in the legs and back, but the giving way of the arches was undoubtedly due to hypothyroidea and general asthenia. The disease here appears in a nullipara; there is a typical myxœdematous ring about the lower ribs; the hair has disappeared from the axillæ, and the skin reflexes cannot be elicited.

Cushing[10] says that if we will watch more carefully we may often identify symptoms of hyposecretion of the hypophysis due to its indirect involvement in cerebral neoplasms. Thus we may account for the marked increase in weight, the amenorrhœa, and somnolence not infrequently seen with these disorders. This may be the explanation of the unusual symptoms in the case just described. This woman has had a marked increase of weight; there has been complete amenorrhœa for several years; the sexual organs have been seriously affected, as she has never conceived, and undoubtedly has had many opportunities to do so. Somnolence has been observed in many cases of myxœdema, and is associated with the mental hebetude, but it is rarely complained of in hypothyroidea. The paresis of the tongue and face points to some old trouble at the base of the brain. Several cases of mxyœdema have been reported in which a nasal optic atrophy and other findings suggested hypertrophy of the hypophysis.

The next case is not typical of hypothyroidism, but is one in which the wonderful improvement seemed to prove that the exaggerated symptoms of the menopause were due to insufficient thyroid secretion. It is all the stranger when we consider that hot flushes, rapid pulses, sweating, and insomnia are symptoms rather of hyperthyroidism. This case showed the great danger of the patent antifat remedies which contain thyroid. This woman was in a critical condition after taking four grains a day for five days. Since then I give only enough capsules for two or three days, so that the patient has to return for observation. It would seem that persons with hypothyroidism are especially sensitive to thyroid extract, as experiments on normal subjects have shown but slight disturbance even after enormous doses.

CASE III.—C. F., French; a cook; widow; aged forty years; complains of "rheumatism," dyspnœa on exertion, and great mental depression. She has always been healthy and a hard worker up to the last year. She has one daughter aged eighteen. Men-

[10] Jour Amer. Med. Assoc., 1909, liii, 249.

struation was normal up to six months ago, when it suddenly stopped. She began to get gray at an early age.

Three years ago her legs began to swell, especially in the afternoons, and for the last year she has been unable to work on account of asthenia and dyspnœa on exertion. She has rheumatoid pains in the larger joints, especially those of the lower extremity; there is persistent backache and the characteristic giving way of the knees. Since the sudden stoppage of the menses she has had hot flushes and perspires excessively. She has become very sad and morbid, with strong suicidal tendencies. There is obstinate insomnia, and the sleep obtained is not restful. Her memory has become very poor, and she has had hallucinations of hearing.

The patient is a short, stout, intelligent woman, with a sad, tired face. The thyroid gland is very small. The supraclavicular fossæ are well filled with fat, but there are not the characteristic pads. The lungs are clear and the heart apparently normal. The pulse is regular and 90 per minute. There is a relaxed vaginal outlet, with slight retroversion of the uterus, and a large cervix with an erosion and considerable discharge. There are varicose veins on both legs, with slight œdema. The plantar arches are in good condition. Urine analysis shows no albumin, sugar, or casts. The blood is practically normal except for 85 per cent. of hemoglobin and slight poikilocytosis.

The pelvic organs were restored to a healthy condition, the varicose veins were supported, the hemoglobin was brought up to normal, and satisfactory sleep was secured, and still the patient was in practically the same condition, unable to do any work on account of the pains and weakness, and suffering from a mild melancholia. On account of the few symptoms of hypothyroidea, she was given two capsules of thyroid a day. She returned in five days with her clothes hanging about her. She had lost nearly twenty pounds and was very nervous, with a pulse of 120 per minute. Thyroid was immediately stopped, and she gained a few pounds. Her whole disposition seemed to change; she forgot her fears and troubles, and as her strength returned she went to work with her old energy. During the next two months she occasionally needed a little thyroid, but, like most of these cases, she reacted very quickly, and the dosage had to be small and carefully watched.

Some of the severer and older cases do not react well to the treatment, probably because permanent changes have been wrought throughout the body. For the same reason, thyroid seldom has any effect on older cretins. Modern surgery may soon come to the aid of these hopeless cases. Payr achieved an excellent result by transplanting a large piece of the mother's thyroid into the spleen of a myxœdematous child, who had derived no benefit from two years of thyroid feeding. Lately, under Kocher's direction, pieces

of thyroid have been successfully transplanted into the epiphyseal junctions of the long bones of animals, and have there taken up their function. Salzer has been repeatedly successful in transplanting thyroid tissue into the abdominal wall of rabbits.[11] Carrel has recently discussed the problems involved in these transplantations.[12]

Symptoms of thyroidism are probably met with much more frequently than those we have just been studying, and the interpretation is still more difficult. A true case of Graves' disease, with marked exophthalmos, tachycardia, tremor, and asthenia, is easy enough to diagnosticate, but when a girl is overemotional, with a rapid pulse, sweats, occasional diarrhœa, and sometimes a little fever in the afternoons, one is more likely to think of hysteria, incipient tuberculosis, or anemia. And even if we recognize the symptoms as those of thyroid overaction, the important questions remain: What is the cause? Is it a transient affair due to some intoxication, or are there changes in the gland which will progress until they induce true exophthalmic goitre? We have yet to obtain a sufficient number of life histories of such cases to prognosticate the dangers of these mild toxæmias. When an attack of scarlatina leaves a girl with scarred and damaged kidneys, we are fearful for the outcome of a pregnancy or an attack of pneumonia. By analogy, the weak spot in these persons would be the thyroid gland, and any extra strain such as shock or infection would be more liable to bring on Graves' disease or other disasters.

Fortunately, we need have no such fears for most cases of hypothyroidea, as it does not tend to go on to the complete form, and spontaneous recovery is probably very common. Another point to be noted is that the thyroid given probably stimulates the gland to take up its work again, otherwise medication would have to be continued indefinitely as in operative myxœdema.

A. R. Elliot[13] mentions as a cause of thyroidism the venous engorgement of the thyroid in heart affections, particularly lesions of the mitral valve. In advanced cases, it may be difficult to tell which is the primary lesion. He describes a toxic form seen in the anemias, digestive toxemia, syphilis, diabetes, and Bright's disease. If it be proved that chronic nephritis can be the cause of thyroidism, we may have another explanation of the exophthalmos seen in that disease. Dr. Barker has observed this symptom in 16 out of 33 cases studied in the Johns Hopkins Hospital.

The following history portrays a case in which a mild thyroidism, following a mental shock at the age of twelve, probably predisposed the patient to a thyroid instability, which was brought out in later years by syphilis.

[11] Arch. f. klin. Chir., lxxxix, 1909. [12] Surg., Gynec., and Obstet., 1909, viii, 606.
[13] Loc. cit.

CASE IV.—G. de V., Mexican; married; aged thirty years; complains of general weakness and nervousness. She was perfectly well up to the age of twelve, when she became inconsolable over the sudden death of both parents. She then suffered from substernal oppression, extreme nervousness, tremor, and hot flushes, and for awhile her friends noticed a staring expression of the eyes. These symptoms disappeared of themselves, and though a tendency to weep at any provocation remained, she has enjoyed fair health until three years ago, when she married a man with late secondaries. She has never conceived, and so far as can be ascertained has had no symptoms of syphilis besides mucous patches. For the last year she has been a nervous wreck, spending most of her time helplessly in bed. She has grown very thin; her appetite is *nil*, and constipation is extreme. She sweats excessively, especially from the hands, but generally keeps wrapped up closely on account of a sensitiveness to cold. She sleeps very little, and then frequently awakes with spasm of the larynx and a fear of choking to death.

The examination revealed a small, thin, nervous, intelligent woman, wrapped up in bed and perspiring profusely. She has considerable gray hair, and has had some for several years. There was no exophthalmos; the lungs were clear; the heart not enlarged, and the sounds normal. Pulse, 50 per minute and regular; blood pressure, 160 mm. of mercury. The pelvic organs were apparently normal. The thyroid was enlarged, the right lobe reaching as far as the clavicle, and overlaid with markedly pulsating bloodvessels in its upper part. The left lobe was the size of a large hazel nut. There was 85 per cent. of hemoglobin. Otherwise the blood was normal. The urine contained no albumin.

She was taken from her bed, given psychic and general tonic treatment, and was soon taking regular exercise and getting stronger. Then extrasystoles appeared, and for the next few weeks she exhibited every form of regularly irregular heart, and would change suddenly from one form to another and back to normal again for awhile. Her strength continued to improve, but she became very nervous and frightened over the pauses after the extrasystoles and the slowness of the pulse, which would drop to forty per minute at the wrist. The only thing that gave any relief was sodium nitrite, which lowered the high blood pressure, but a severe cold left her worse than before. About that time the husband confessed that he had had active lesions at the time of his marriage, and was still in need of aggressive treatment. They were both put under treatment, and the wife steadily regained her health, so that now she does her own housework. The pulse became normal in rate and rhythm, and the thyroid decreased in size. She is still greatly affected by colds, which upset her entirely and cause a recurrence of the nervousness, tremor, and irregular heart.

The next case is one of those in which symptoms of hyper-

thyroidism occur in a woman with an old, previously innocuous goitre.

Case V.—L. K., Mexican; widow; aged thirty-five years; complains of difficulty in speaking and swallowing, and a burning in her throat. Menstruation began at the age of fifteen, and was regular, scanty, and always painful. Married at nineteen, she has had three children, who all died in infancy. There were no abortions. A goitre appeared coincident with the first pregnancy, and grew fast enough to be very noticeable at the birth of the child. There was tremor, weakness, and nervousness, but no exophthalmos.

After a long period of quiescence, the tumor is slowly growing again, so as to affect her voice and swallowing. It also causes a dry hacking cough. She is very nervous and depressed, and cannot sleep. She has grown thinner and weaker, and her knees give way from under her. She menstruates slightly for a day or two, and often misses periods. There is persistent pain in the left hypochondrium. She feels cold all the time; never sweats, and the skin is so dry that her stockings are full of scales. She has annoying hallucinations of hearing, and sometimes tinnitus. She cannot look upward without a drawing sensation, and the lids feel as if held shut. Constipation is extreme. There is very little dyspnœa on exertion, and the heart's reserve force seems to be good. There is occasionally slight swelling of the feet.

The patient is a tall, thin, sad-looking woman, whose intelligence seems to be considerably impaired. Slight exophthalmos gives a staring expression to the eyes. There is no tremor. The voice is harsh, and she speaks as if the mouth were full of food. There is a large rubbery goitre. The heart is slightly enlarged, and there is a loud systolic murmur best heard at the apex, but also all over the precordium. The second pulmonic sound is accentuated. The pulse ranges from 100 to 120 per minute, is of small volume, and generally regular in force and rhythm.

The treatment was entirely unsatisfactory, as she did not react to anything. Even six drams of sodium phosphate a day had no effect on the constipation. Sedatives and rest produced no effect on the nervousness, and nothing relieved the burning in the throat. Thyroid was tried without any result.

In this and the preceding case, hyperthyroidism was predominant, but at the same time there were several symptoms that usually occur with incomplete myxœdema. In the first case, there was slow pulse, with high blood pressure, irregular, however, and susceptible even to changes in position; chilliness; spasms of the larynx and premature grayness; in the second, pain under the left breast, coldness, dry skin, hallucinations, and tinnitus.

It has long been known that a case of exophthalmic goitre can progress through a mixed indefinite type even to typical myxœdema. These stages correspond to advancing pathological

changes in the thyroid gland. At first there is simple hyperemia and slight change in the colloid; then there is cellular hyperplasia and increase of the colloid. The cellular hyperplasia goes on, there are imperfect alveoli lined with large cells, and the colloid nearly disappears. In the last stage there is fibrosis, atrophy of the cells, hemorrhages, and cysts.

Rogers and Beebe[14] emphasize the complexity of the treatment in the indefinite cases, and report several instances in which improvement was obtained only by simultaneous administration of small doses of thyroid protein and their specific serum. They advocate the use of the purified thyroid protein in very small doses, $\frac{1}{50}$ grain or less, and they believe that it will give results when the desiccated thyroid will not. The latter may be given in $\frac{1}{4}$ grain doses, and even then carefully watched. They enumerate the following types that may require combined treatment:

1. Patients who develop thyroidism late in life: (*a*) Those who, after middle life, show thyroidism for a varying period before the appearance of a goitre. (*b*) Those who have borne an innocuous goiter for years, and late in life develop signs of thyroidism.

2. Atypical forms of thyroidism: (*a*) Generally women of any age who present many signs of thyroidism, but who often have a dry skin and bradycardia, and are usually considered neurotic and neurasthenic. (*b*) Patients with nervous and vasomotor signs of thyroidism, but who complain of a more or less constant headache, accompanied in most cases by nausea and abdominal discomfort. (*c*) The psychopathic cases.

It is to be hoped that their serum will be perfected and made easily procurable, as the mild cases of thyroidism are quite common and react very poorly to the usual sedative treatment. These are the cases in which they obtained the largest percentage of complete success, with the most prompt and striking results, probably because there are no complications and no lasting changes in the gland. Ordinarily these patients are given rest and tonic treatment and recover only to relapse on getting up. Sometimes they seem to do better with moderate exercise in the open air, but they will only be relieved, and any little cold or indigestion will cause them to lose all they have gained.

Juvenile Myxœdema. When confronted with a fat stupid-look-looking child, stunted in mind and body, one has to think of several conditions, such as Mongolian idiocy; chondrodystrophy, which produces the typical dwarf; dystrophia adiposogenitalis of Fröhlich,[15] caused by tumor of the hypophysis; cretinism; and juvenile myxoedema. The last named disorder causes a late cretinism, and seems to bear the same relationship to cretinism that hypothyroidism does to complete myxœdema.

[14] Arch. Int. Med., 1908, ii, 297.

[15] Wien. klin. Rundsch., 1901, 47, 48.

It is seen more frequently in boys than in girls, and often follows an attack of measles. The development is retarded, and there is a tendency to obesity and a protuberant abdomen. As a rule, the intelligence is but slightly impaired. Walking, talking, and dentition are apt to be delayed, and the teeth may be erupted carious. Adenoids are frequent and help to keep the thickened lips separated, while the swollen tongue protrudes and gives a characteristic look to the face. The following case would probably fall under this classification.

CASE VI.—C. C., a Mexican boy, aged seven years, is brought by his parents to ascertain the cause of his inability to speak above a whisper. The histories of both families are good. The father and his brothers all speak thickly. There were fifteen children, of whom thirteen are living, and all are healthy but two—this one, and another who had convulsions when eight days old and has grown up hydrocephalic and mute. Infectious diseases caused the two deaths. This child has always been healthy except for an attack of varicella. He walked at fourteen months, and did not begin to talk until two years old. His intelligence has been about the average. He has always been very morose and unapproachable, and does not form friendships with other children. They torment him with the nickname "Japones," on account of his resemblance to a Japanese child. In December, 1907, he had a slight attack of measles, from which he made an uneventful recovery. Five days later he was a little hoarse, and since then has not spoken above a whisper.

The boy is a little small for his age; his bones are well shaped and sized; he is a little too fat, and the abdomen is protuberant; the skull is well shaped, and the fontanelles are closed. The palpebral fissures are not oblique, and the Mongolian expression is produced by the large tongue protruding between his lips and the general facies of cretinism. He is very surly, and speaks only in whispers. There are a few small adenoids. The nose is quite normal. Hearing is slightly impaired. The vocal cords appear to be normal in every respect, and there is no paralysis. No thyroid can be felt. The hands are pudgy, with short fingers. The teeth show a most remarkable condition in that there is almost no enamel to be seen on any of them. His hair is coarse and straight.

A grain and a half of thyroid a day was given, and the boy has slowly recovered his speech and become more like a normal child.

One of the most confusing things in the study of these disorders, and one that has caused much difference of opinion, is the intimate relation of all the ductless glands one to another. Hence one must always keep in mind that the symptoms observed after the extirpation of one of these organs may be due not only to the loss of that organ, but to changes, compensatory or otherwise, in the remaining glands and their internal secretions. For the clinician also, difficulties are placed in the way of assigning certain symptoms to the complex of one particular gland.

Falta lays particular emphasis on this intimate relation, and compares a pathological process in one of these organs, and its effects on the others, to the associated changes observed in derangements of a part of the hematopoietic system. In his Oration on Surgery at the last meeting of the American Medical Association, Cushing[16] said: "It is impossible to remove—probably partially to remove—the hypophysis without producing marked alterations in all the other glands—thyroid, parathyroid, adrenal, testicle, ovaries, islands of Langerhans, and thymus."

Changes in the hypophysis after castration or thyroidectomy are well known, and now the reverse has been found true—there is acute hypertrophy of the thyroid after hypophysectomy, and sexual power is lost in all affections of the hypophysis. A careful study of 122 cases recently reported by Erdheim and Stumme goes to prove that the hypophysis increases in size and weight with each pregnancy, and at last remains enlarged. They think that this may account for the swollen face, lips, and hands sometimes seen in the later months of pregnancy. The symptoms of hypopituitarism may closely resemble those of hypothyroidea—adiposity, polyuria, shedding of hair, and lessening of sexual activity. Castration will produce adiposity, and the symptoms of the menopause may be those of thyroidism. Injury to or loss of the parathyroids produces some of the symptoms that were formerly considered of thyroid origin, and we may yet distinguish and separate some more. The spasms of the larynx, the rheumatoid pains, and the loud cracking of the joints sometimes present in hypothyroidea have all been observed in hypoparathyreosis. On account of the close relation of the parathyroids to the thyroid, they could easily be affected by pressure or by the same pathological process that affects the larger gland. There is also a chemical relation that may be affected, as it has been shown that in thyroidectomized dogs, the effects of adrenalin are much diminished, but if the parathyroids are also removed, the action is increased.

Excepting confinements, probably 95 per cent. of the night calls in this part of Mexico are for "ataques." The subject is almost always a woman, generally young and frequently a sufferer from the mild forms of thyroidism. They may be convulsions, twitching, chattering of the teeth, and substernal pain and oppression, but the most characteristic symptom is the numbness that may travel from one extremity to another, or remain in an arm, or leg, or one half of the body. At first sight, these attacks would be put down to hysteria, but when the sober mother of a family awakes suddenly at night with an "ataque," one feels the need of an etiology more definite than the word hysteria. Anyone seeing a case like that re-

[16] Loc. cit.

ported by Halsted,[17] without the history of a recent complete thyroidectomy, would probably call it hysteria. The resemblance of those "spells" to many seen here is very striking. In this connection, it may be worth while to relate the following case.

CASE VII.—The patient was a stout Mexican woman, aged twenty-four years, who had always enjoyed good health and whose menstrual life had been normal. Her illness began a week after her wedding, when she flowed profusely for three weeks. Some symptoms of thyroidism developed—tachycardia, tremor, enlarged thyroid and sweats, and occasional attacks of vomiting. She had several attacks with numbness, twitching, and fear of impending death, and she spent three weeks of every month in bed, on account of the excessive flow and nervousness. In spite of the hemorrhages and thyroidism, she gained in weight, and the lowest point reached by the hemoglobin was 65 per cent. She was treated by several physicians, and nothing had the slightest effect upon her condition. The pelvic organs were apparently normal, and curettement was refused. One day, in taking a blood smear, it was noticed that the blood clotted very slowly, and calcium chloride (the only salt then obtainable) was given as an experiment. The effect was marvellous. The flow stopped in a few days, and in a month she was a strong, capable woman, with complete control over her nerves and a normal pulse. Treatment was continued over another menstrual period, which was normal. She had remained perfectly well for over a year, but has never conceived. She is still very stout. Calcium was given here as an experiment with the hope of a temporary relief only, but it seemed to be the cause of the marvellous change in the patient's condition. Possibly an overexcitation of the ovaries caused them to functionate to excess and to implicate the thyroid, and directly or indirectly the parathyroids. The calcium administered may have affected the glands in the reverse order and established a balance.

Since studying the case just described, I have been trying to elicit the Chvostek and Trousseau signs just after patients have calmed down from an "ataque," and find that twitching of the lower part of the face can be induced by a modification of the Chvostek sign. The region just in front of the tragus is firmly rolled under the finger instead of striking, which would often be considered an indignity by the ignorant relatives. Of course this sign reveals simply the hyperexcitability of the muscles and nerves.

It may be some time before we get active extracts from every one of the ductless glands, but we may learn how to use their correlation to advantage so that we can treat the individual gland by restoring the balance of the system.

[17] AMER. JOUR. MED. SCI., 1907, cxxxiv, 1.

TYPHOID SPERMATOCYSTITIS AND PROSTATITIS, AND THEIR RELATION TO CHRONIC TYPHOID BACILLURIA.

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Individuals who have passed through an attack of typhoid fever may carry in their gall-bladder, urinary channels, or intestinal tract living virulent typhoid bacilli for an indefinite period of time. These people are termed "chronic bacilli carriers," and it is by excretion of the bacilli from these cases that typhoid fever is largely spread. It is not necessary that extensive pathological changes should be present in their organs; but, on the contrary, the slightest catarrh or the smallest amount of infiltration of the respective mucous membrane lining these organs often exists. It has been shown by Petruschky[1] that the urine is the great spreader of typhoid bacilli, and is probably more dangerous than the feces. Typhoid bacilli are often present in the urine in enormous numbers, and may remain for months or years without causing any symptoms. As a rule, they are the sole microörganism present. Apparently healthy people may have typhoid bacilli present in the urinary bladder and excrete them in the urine for a long period of time.

There have been cases in which the bacilluria was of extremely long duration, such as a case described by Liebetrau,[2] in which after nine years the bacilli were found in the urine, and a case reported by Houston,[3] in which the bacilli were isolated after three years. Gwyn[4] relates a case of typhoid fever treated in the hospital and discharged; the patient entered the hospital five years later with cloudy urine, the examination of which showed numerous typhoid bacilli. There are many other cases on record in which individuals have gone about the country a menace to the whole community.

It is generally supposed that, during the course of an attack of typhoid fever, typhoid bacilli circulating in the blood are excreted by the kidneys, and that the bladder urine serves as a culture medium in which they multiply rapidly. However, a simple or physiological excretion of microörganisms by the healthy kidney, with their appearance in the urine, has been shown by experiments in animals by Wyssokowitsch[5] not to occur; the kidneys always show focal lesions. The studies of Konjajeff[6] on human subjects is in accord

[1] Centralbl. f. Bakt., 1898. xxiii, 577.
[2] Arbeit a. d. Kaiser Gesundheitsamte, 1906, xxiv, 341.
[3] Brit. Med. Jour., 1899, i, 79.
[4] Johns Hopkins Hosp. Bull., 1899, x, 109.
[5] Ztschr. f. Hygiene, 1886, i, 3.
[6] Ref. Cent. f. Bakt., 1889, vi, 672.

with the animal experiments of Wyssokowitsch. He found at autopsy in typhoid fever cases small focal lesions in the cortex of the kidney, which he proved began by the lodgement of minute emboli in the smallest bloodvessels. These emboli were composed of bacilli and produced a necrosis of a circumscribed area of kidney tissue. The foci often communicate with the kidney tubules and lead to bacteria passing into the urine. The sudden appearance of typhoid bacilli in the urine late in the disease as in convalescence is especially of interest, and speaks for the late breaking into the urinary channels of the kidney lesion.

There have been a few instances in which the urine has become infected with typhoid bacilli in other ways. The possibility of infection taking place from without the urethra in the same manner as with Bacillus coli, or the streptococcus, has been suggested in Houston's case. Brown[7] reports a case which was infected by the passage of a catheter. Blumer[8] has suggested that typhoid bacilli may pass through the posterior vesical wall from the intestinal tract in the same way as Lesieur[9] has shown that bacilli may enter the wall of the intestine, sometimes without producing a definite lesion. Jacobi,[10] who observed four cases of long-drawn-out bacilluria, concluded that a nephritis was present and was often complicated with a hemorrhagic nephritis; and, moreover, his cases helped to prove that typhoid bacilli are only excreted by a diseased kidney There were cases, however, reported by this author in which no albumin was present in the urine although typhoid bacilli were found.

These cases have received special study, and many observers have advised giving typhoid-fever convalescents some bactericidal drug, which in general causes the bacilli when present in the urine to disappear. But there are cases in which typhoid bacilli disappear from the urine when such drugs are given, and reappear at the end of a few weeks when treatment is stopped. The reasons for this condition have not always been clear. The bacilli in the case of Richardson[11] disappeared three times, and reappeared each time after treatment. Horton Smith,[12] Connell,[13] and others have called attention to the recurrence of bacilluria after treatment in this manner; in these cases an ulcerative cystitis has been present, furnishing the source of urinary infection.

At the suggestion of Professor Ludwig Pick I have made a study of two cases of typhoid fever which presented anatomical findings of extreme interest when considered in relation to urinary infection. The first case showed an acute typhoid spermatocystitis, and the

[7] Edin. Med. Jour., 1905, xix, 116. [8] Johns Hopkins Hosp. Rep., 1895, v, 327.
[9] Hygiene gén. et appliq., Paris, 1906, i, 536.
[10] Deut. Arch. f. klin. Med., 1902, lxxii, 442.
[11] Jour. Exper. Med., January, 1899. [12] Lancet, 1900, p. 915.
[13] Amer. Jour. Med. Sci., May, 1909.

second case an acute typhoid prostatitis. Both of the subjects entered the hospital with the diagnosis of typhoid fever and went to autopsy. I am indebted to Prof. Dr. Stadelmann, director of the hospital, for the histories of the cases.

Case I.—The patient was a man aged seventeen years, who entered the hospital with the diagnosis of typhoid fever. On account of his comatose condition an exact history could not be obtained. It was learned from the mother that he had been in poor health for a week, and had some headache and cough. The family history was negative. The mother believed the present illness to be of about fourteen days' duration. The patient was in the hospital for nine days in a semicomatose condition with severe typhoid symptoms, and finally died from perforation.

The autopsy made by Professor Pick showed: Typhoid ulceration in the ileum with perforation, fibrinopurulent peritonitis, cystitis with small hemorrhage in the urinary bladder, purulent spermatocystitis and right deferenitis, ulcer on the epiglottis, parenchymatous nephritis with miliary abscess, obliterative pleuritis and diffuse bronchitis, and aspiration of stomach contents.

The detailed findings in the seminal vesicles, were as follows: The seminal vesicles are somewhat enlarged, the right more than the left; both fluctuate. On the outer surface they are reddened. The left seminal vesicle is filled with a more grayish fluid. The vas deferens contains likewise some thick yellowish fluid. On the right side the vas is normal. By pressure from behind on the penis no secretion can be pressed out. The urethra is smooth and pale. The prostrate gland shows no changes.

From the purulent material taken from the seminal vesicles plates were made by Professor Pick upon agar and Conradi-Drigalski media, from which were obtained numerous colonies of a living motile bacillus with the following cultural characteristics: Litmus milk was not coagulated, neutral red was not reduced, no gas was formed, the growth upon potato was not visible, and upon Conradi-Drigalski media blue colonies were formed. Controls were made with typhoid and colon bacilli upon the above culture media, and typical growths were shown. From the growth upon culture media it was seen that we had to do with an organism that has the same cultural characteristics as the typhoid bacillus. The agglutination tests were carried out with the following results: In a dilution of 1 to 10, 1 to 100, and 1 to 1000, the bacilli were killed and clumped completely within ten minutes. In a serum dilution of 1 to 2000 and 1 to 5000 the organisms were clumped within ten miutes. Controls were made and were negative, including the reactions with a known culture of paratyphoid *a*. Injection of the culture into guinea-pigs showed a lessened virulence. The behavior in animal experiment was the same as is produced when cultures of typhoid bacilli are injected.

The histological findings of this autopsy are of extreme interest in relation to the seminal vesicles. Section of the left seminal vesicle shows the mucosa in many places to be destroyed, and in others distorted and infiltrated. The lumina are dilated and filled with an acute cellular exudate which is partially necrotic. The exudate is composed of many polymorphonuclear leukocytes, plasma cells, lymphoid cells, and, besides these, are found desquamated epithelial cells from the lining of the gland. There are present round cells in the submucosa in irregular heaps infiltrating the connective tissue.

FIG. 1.—Section of seminal vesicles from Case I, stained with carbol-fuchsin, showing breaking down of epithelial cells, in which clumps of typhoid bacilli are seen in the lumen of the gland. (1/12 oil immersion, ocular No. 8.)

When these sections were stained with carbol-fuchsin and decolorized with alcohol, by careful search, rod-shaped bacilli were found lying in the lumina of the glandules (Fig. 1.) Sections stained by Gram show that these microörganisms are negative to that stain. In their morphological and staining characteristics these bacilli are identical with typhoid bacilli.

CASE II.—A male, aged twenty-eight years, was admitted to the hospital with a diagnosis of typhoid fever of about ten days' duration. Death took place from hemorrhage of the bowel four days after admission.

The autopsy by Professor Pick showed: Typhoid ulcerations in the ileum, universal icterus, subepicardial and subpleural hemorrhages, acute tumor of the spleen, parenchymatous nephritis with

small abscesses, acute purulent prostatitis, swelling of the mesenteric lymph glands, and acute catarrh of the duodenum.

The important feature of this case was the condition found in the prostate, which was as follows: The prostate gland is of rather large size, the right lobe being the larger. In the lobes is an area the size of a bean containing a purulent, yellow, granular material upon a reddened floor. By pressure upon the lobes, pus exudes. The testicles and epididymis are free from change. On the left side is a small hydrocele. The seminal vesicles are moderately filled and on the outer surface injected. The inner surface of the seminal vesicles is not injected.

In this case cultures were made by Professor Pick from the spleen, gall-bladder, lymphatic glands, and from the purulent material expressed from the prostate gland. From the spleen, lymph glands, and prostate, a living motile organism was isolated, which on Conradi-Drigalski media showed blue colonies, produced no gas and no indol; neutral red was not reduced, litmus milk was not changed, and milk was not coagulated This organism, therefore, in its cultural characteristics was identical with the typhoid bacillus.

Further tests were carried out with the strain isolated from the prostate gland as follows: A guinea-pig, 275 grams in weight, was injected with 1 to 2 c.c. of a twenty-hour-old culture. The animal was not killed. Further animal experiments showed that in its behavior this culture is the same as cultures of the typhoid bacillus. Agglutination tests were carried out with typhoid agglutination serum. This organism isolated from the prostate gland was agglutinated by the following dilutions of this serum: With a serum dilution of 1 to 100, 1 to 1000, and 1 to 2000 the organism was killed and completely clumped in less than ten minutes. In a dilution of 1 to 5000, 1 to 10,000, and 1 to 20,000 the organisms were killed and clumped in fifteen minutes at 37° C. All controls necessary were made, including reactions with paratyphoid *a*, and gave negative results. Additional agglutination reactions were carried out with the organism isolated from the mesenteric lymph glands, and identical results were obtained as with the organism isolated from the prostate.

Histological examination of sections from the various organs from this autopsy were made. Of great moment were the findings in the prostate gland. Section of this shows an acute purulent exudate with breaking down of the glandular cells. In this exudate can be seen, when the sections are stained with carbol-fuchsin and decolorized with alcohol, bacilli lying singly and in small groups (Fig. 2). These organisms, which present the morphological characteristics of typhoid bacilli, are Gram-negative.

There is no doubt but in both of these cases were examples of genuine typhoid infection. The first case showed living, virulent typhoid bacilli in the seminal vesicles while the prostate gland was

free. The second case showed the typhoid bacilli in the prostate gland with normal seminal vesicles. The bacilli in both cases were in the lumina of the glands outside of the secreting cells.

The findings in these two cases at autopsy has led to the suggestion that the seminal vesicles and the prostate may be infected in patients who have typhoid fever. From the location of the typhoid bacilli in the stained sections, and because of the fact that some infections of the prostate gland and seminal vesicles have a tendency to assume a chronic character, there is reason to believe that in subjects recovering from typhoid fever, the prostate gland and the seminal vesicles may sometimes harbor typhoid bacilli for a long time.

FIG. 2.—Section of prostate gland from Case II, stained with carbol-fuchsin, showing breaking down of the normal structure. Two rod-shaped organisms (typhoid bacilli) are seen in the centre of the section. (1/12 oil immersion, ocular No. 8).

It can easily be assumed that the bacilli may readily pass into the urethra with the semen as in the first case, and with the prostatic secretion in the second case, reach the urinary bladder, and produce a typhoid bacilluria. In this way we may explain the recurrence of typhoid bacilluria on the suspension of treatment, and also the fact that no clinical signs of kidney lesions are found in these patients. Clinically, therefore, in patients with typhoid bacilluria, the possibility of infection of the urine from these lesions in the prostate gland or seminal vesicles should be considered. In long-continued bacilluria, especially in patients in whom the micro-organisms disappear under treatment and then reappear at a later

period, and also in "chronic bacilli carriers" in whom the excretion of typhoid bacilli is by way of the urine, the attention of the clinician should be directed to these organs as offering a source for the distribution of the typhoid bacillus.

In conclusion, I extend my heartiest thanks to Professor Ludwig Pick for the suggestion and opportunity of carrying out this work.

VON GRAEFE'S SIGN IN MYOTONIA CONGENITA (THOMSEN'S DISEASE).

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The congenital familial myopathy which is characterized by stiffness or hypertonicity of the voluntary muscles upon attempted motion, peculiar electrical reactions, and a chronic course little affected by treatment, has, in most of its manifestations, been sufficiently discussed. Although this condition was described by Leyden[1] in 1866, the classical description by Thomsen[2] has been the basis of most of the subsequent study. The most valuable addition to this subject since Thomsen's is the careful work of Erb,[3] with the announcement of the peculiar electrical reactions of the muscles of the myotonics.

The present study was undertaken because of the observation of a family with a history of marked von Graefe sign for five generations. The von Graefe sign is so evident that it is considered by the family the most interesting manifestation of the condition, and the underlying myotonia had gone undiagnosticated through several generations.

Most of the descriptions of these cases do not mention the eyes at all. Many reports state definitely that the eyes were not affected.[4] The pupillary reflexes are stated to be normal by several.[5] Squint,[6]

[1] Deut. med. Woch., 1892.

[2] Arch f. Psychiat., 1875-76, vi.

[3] Deut. Arch. f. klin. Med., 1889, xlv.

[4] Peters, Deut. mil.-ärztl. Ztschr., 1879, viii; Petrone, Riv. sper. di freniat, 1881, vii; Weichmann, Inaug. Diss., Breslau, 1883; Schönborn, Deut. Ztschr. f. Nervenh., 1889, xv; Cook and Sweeten, Brit. Med. Jour., 1890; Bernhardt, Virchow's Arch. f. path. Anat., lxxv; Haynes, Jour. Nerv. and Ment. Dis., 1897; Pelizaeus, Centr. f. Nervenh. u. Psychiat., 1897; Gessler, Med. Cor.-Blt. Würt. ärztl. Ver., 1898, lxviii; Mele, Gio. med. d. esercito, xlvi. 1898; Hoffman, Festschr. W. Erb, 1900; Brinckmann, Inaug. Diss., 1902; Braun, Inaug. Diss., 1902; Modena, Riv. sper. di freniat, 1905; Curschmann, Berl. klin. Woch., 1905.

[5] Schönfeld, Berl. klin. Woch., 1883; Delogu, Gazz. d. osp., 1897, xviii; Rizzoti, Boll., d. clin. 1903; Carncross, Jour. Nerv. and Ment. Dis., 1903; Seeligmüller, Deut. med. Woch., 1876.

[6] White, Guy's Hosp. Rep., 1889; Wichmann, Neurol. Centr., 1897, xvi; Meara, Arch. Pediat., 1905.

diplopia,[7] inequality of the pupils,[8] emmetropia,[9] nystagmus,[10] and a jerking motion upon following the finger,[11] are mentioned in various cases. Thomsen himself observed that the facial muscles are affected, and made special mention of the orbicularis palpebrarum. That the eyes are opened with difficulty is frequently stated.[12] Messaroch speaks of the eyes closing with difficulty. More or less humorous conditions are described by several observers: the eyes remain closed upon sneezing[13] or after washing. Westphal and others[14] mention involvement of the external eye muscles, and Bechterew[15] cites a case in which the patient had to open his eyes with his fingers. Preston[16] speaks of the eyes "setting." Hlavaczek and Jacoby[17] refer to the "catching of the eyes."

After a careful search I have been able to find but one notation of the von Graefe sign, in connection with myotonia congenita, and that is by Oppenheim in his text book on nervous diseases; he states that he observed such a case, and says that the fact was confirmed by Mann. This was, however, a single case, and it is not stated that the sign occurred through several generations as the salient feature.

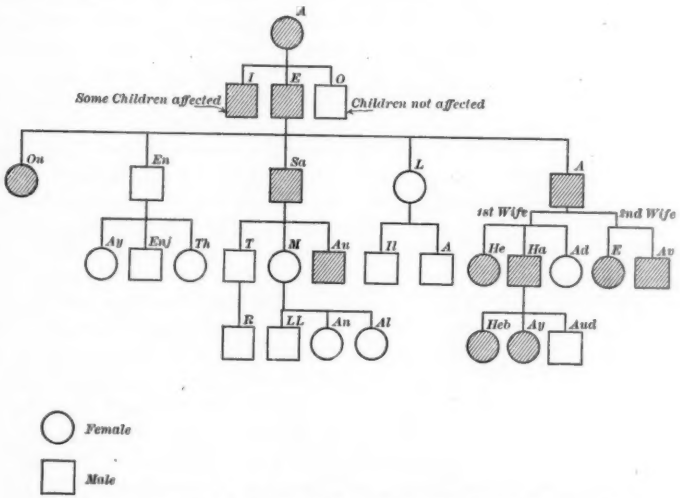
Buzzard[18] says of one of his cases: "Occasionally his eyelids will become partly fixed in a half-open position, so that for an instant he can neither open them further nor shut them." In Preston's case: "When he looked fixedly at an object his eyes became set." "At times his eyes rolled up to such an extent that only the whites were visible." Meara describes one of his cases as follows: "The eyes show a convergent strabismus. The father says that before the glasses were prescribed (a year ago) he was accustomed to carry his head down with the eyes turned downward, and when he wished to look up he would lift his head, and then the whites of his eyes could be seen. The eye condition could readily be attritubed to the stiffness of the ocular muscles." Messaroch's patient may have shown something similar to von Graefe's sign. He says: "When the eyes were opened exceptionally wide, it was not possible for him to close them at once, that is, in changing the direction of vision." Ballet reports an interesting involvement of the ocular muscles, but in an "acquired" case of myotonia.

The family whose chart of descent is here presented is of the oldest New England stock. Of the twenty-nine members recorded,

[7] White, loc. cit.
[8] Hoffman, Deut. Ztschr. f. Nervenh., 1896. ix.
[9] Mahler u. Beck, Wien. klin. Woch., 1900.
[10] Raymond, Jour. de méd. interne, Paris, 1902; Pels. Arch. f. Psychiat., 1906-07, xl.
[11] Eulenberg u. Melchert, Berl. klin. Woch., 1885; Angell, Jour. Nerv. and Ment. Dis., 1891; Raymond, loc. cit.
[12] Engel, Phila. Med. Times, 1882; Pontoppidan, Neurol. Centr., 1884; Friis, Neurol. Centr., 1892; Benoit, Arch. de méd. et pharm. mil., 1892, xx; Dejerine et Sottas, Rev. de méd., 1895.
[13] Seifert, Arch. f. klin. Med., 1890; Ballet, Progrès méd., 1902; Holemans, Arch. méd. belges, 1905; Messaroch, Allg. med. Centr. Ztg., 1904.
[14] Berl. klin. Woch., 1883.
[15] Deut. Ztschr. f. Nervenh., 1905.
[16] Med. News, 1898, lxxiii.
[17] Jahrb. f. Psychiat., 1895.
[18] Lancet, 1887.

thirteen were affected with myotonia and sixteen were free. All of those affected showed the von Graefe sign to a greater or less degree. Of the affected, seven are males and six are females, a fairly equal division. I have seen no members of the first and second generations among the fourteen of the family that I have observed, but the history of the von Graefe sign is very definitely related by Sa, of the third generation.

The patient Sa, of the third generation, was fifty-nine years old at the time of his examination, July 31, 1906. He was a civil engineer and the son of a New England sea captain who died of apoplexy at the age of forty-six years. His mother died at eighty, of some heart trouble. Two brothers and one sister were living, while one sister died at the age of sixty-one, of yellow fever.



The shaded portions of the diagram indicate those affected with myotonia and von Graefe's sign.

He stated that the following members of the family, who can be found upon the accompanying diagram, were affected with myotonia and manifested the von Graefe sign. In the first generation his paternal grandmother, in the second generation his father and his father's brother, were affected. In the third generation one brother and one sister were affected, while one other brother and one other sister were free. The myotonic brother transmitted it through two mothers to four out of five children. The unaffected brother and sister did not transmit it. None of them, he says, have complained of pain or disturbance of sensation. He had measles and pertussis as a child, and was in bed two days with influenza in 1892, without

complications or sequels. He has been otherwise exceptionally well, strong, and robust. His mentality is excellent.

The trouble with the muscles manifests itself as a "stiffness." There is especial difficulty in relaxing them when they are once "fixed." This is more marked in moist or cool weather, or when he is warm and cools off. He describes the condition as "cramp-like but not painful." He has marked von Graefe sign. He can "feel the upper lid hang back" when he looks down. He notices the condition in the tongue, eyelids, face, mouth, hands, and legs. Relaxation is more difficult than contraction. He has no trouble with the glottis, breathing, or sphincters. There has been little change in the condition since boyhood. If there is any difference, he is better now.

He tells of difficulty which he experienced in hurrying to morning classes at college. When he wished to mount a certain stairway, it was necessary to stop at the beginning of the climb. He would then take out a note book to cover up the real cause for the delay, gradually raise one foot and then the other until under way, when the movements went progressively better. His son attended the same college later, and often had difficulty on the same stairway.

The patient came under observation complaining of loss of appetite for the last eight or nine months, with occasional vomiting and "leg ache" for the last three months. During this time he has lost weight markedly. The myotonia had, however, existed during the whole life, and this condition, which will be referred to later, is a recent manifestation.

Examined on a bright clear day, the patient being under no form of excitement, the only muscles showing the trouble at the examination were of the eye. When the patient looked down, the upper lid did not follow the eyeball at once and a wide strip of sclera was left exposed. He said he feels the upper lid "hang back." Upon attempting to follow a finger downward, the eye went down in a jerky manner, and each jerk made the strip of sclera which was visible wider. The general muscular strength was much above that of the average man of fifty-nine years. The consistence of the muscles was normal. There was no fibrillary twitching.

December 1, 1906, he was examined again by Dr. Shelden. He had lost twenty-two pounds. The nausea, vomiting, and loss of appetite had increased. Physical examination showed nothing further in explanation of the loss of weight and nutritional disturbance. He was well nourished and weighed one hundred eighty-four pounds. His musculature was good and the thorax of normal form. The heart and lungs were normal. The examination of the abdominal organs gave no findings of consequence. The urine was normal and the pulse full, regular, and of normal frequence. There was no goitre. The erythrocytes were 5,013,000 and the

leukocytes 5060 in number. The hemoglobin estimation showed 83 per cent.

An exploratory incision was made in another city in 1907. The gall-bladder was found to contain dark, thick bile, but there was no evidence of carcinoma. The anemia, anorexia, emesis, and loss of weight progressed until his death, in September, 1908, without a postmortem examination or a satisfactory explanation of the cause of the fatal issue.

It is of interest in this connection that some cases have been observed to develop into a form of muscular atrophy.

It will be noticed that this patient was a direct descendant of affected members, and that when once the line is broken by an unaffected member, the descendants of that one are free.

In the fourth generation I have observed M, T, and A unaffected; Au, Ha, and He affected.

Ha, of the fourth generation, is an army officer, aged thirty-three years on August 9, 1909. His mother died at the age of twenty-six years, and one sister died at twenty years in child birth. His father, who was a brother of Sa, had the "cramps" from boyhood, most markedly in the hands and eyes. His father had difficulty in getting up from a chair; that is, he could rise, but his legs would stiffen when erect, and the first step or two would be taken stiff-legged, after which the muscles would "limber up." He also had difficulty in deglutition, especially when he was excited or angry, at which times he would extend his head and protrude the lower jaw, making two or three attempts at swallowing to overcome the difficulty. In spite of the fact that the father has considerable trouble in opening his hands, he is still working actively at his profession of civil engineering.

As may be seen by the diagram, the patient's two sisters, one brother, and two daughters are myotonics. The patient had typhoid fever in 1898, but has otherwise been exceptionally well.

He cannot remember when he did not have trouble with the muscles. He recalls that when he was six or seven years old he tried to start in a race, when the muscles "set," and he fell sprawling. He was soon able to get up again and run. He found it difficult to let go of the ball when throwing.

Aside from the von Graefe sign, which he has to the most marked degree, he has difficulty in getting the eye opened when closed tightly, as in sneezing or shooting. Hot, damp weather, excitement, and rapid motion bring on the tonicity. Speech is not disturbed. To show the effect of excitement, he relates that once when examining prisoners in the Philippines, who were not telling the truth, he rose suddenly to threaten them, his muscles stiffened, he could not relax, and fell against the men. He fell to the floor, got up slowly, less excited, and soon relaxed.

He weighs one hundred and ninety-five pounds, is five feet ten inches

tall, and is a well-nourished, intelligent, active man. The examination of his heart, lungs, and abdominal viscera shows nothing abnormal. When he looks down the eyelids lag behind the balls for an appreciable time, and a wide band of the sclera is plainly shown. This is especially noticeable when he looks up first and then looks down quickly. The pupils react normally and the vision is good.

1. Mechanical stimulation, by tapping the arm, gives a slow, wave-like motion of the muscles.

2. Galvanic stimulation of the left first interosseous provokes a slow, wave-like contraction, the ACC being equal to the CCC.

3. The faradic reaction is good but slow, and is given by a much weaker current than in the normal control muscle.

Patient He, of the fourth generation, was observed in 1902 without the opportunity for physical examination. The von Graefe sign was present. She was an unmarried woman of twenty and a sister of Ha. Her own statement is as follows: "I first noticed the symptoms of this disease when eleven or younger. Sometimes, when running, the muslces above the knees would grow suddenly stiff and I would fall. I have noticed that the muscles of my eyelids are more apt to play me false in damp, cold weather, and sometimes when embarrased, as when meeting strangers as a child. Getting warm and then cooling off rapidly will also cause the eyelids to seem to stick to the top of the eyeballs, while the balls themselves seem to protrude very far. This is not very painful, but very uncomfortable. When this occurs often, the eyes become a little inflamed and have a smarting sensation. They feel strained and tired also. I am either outgrowing it, or do not notice it so much. Other members of the family who are affected in the same way say they are not aware when the eyelids fail to come down over the ball. I always know, and by looking up until the muscles seem to relax, I can overcome it."

Patient Au, the son of Sa, and cousin of He and Ha, of the fourth generation, was twenty-five years old in 1905, and an engineer. His mother is living. One brother and one sister are not affected. The patient had tonsillitis and measles as a child, but has been otherwise well. He has noticed the "stiffness" of the muscles from childhood. It is especially noticeable in the upper and lower extremities and upon cold or damp days. Excitement brings it on. At times he is nearly free from it. He speaks of the difficulty of relaxing and releasing after shaking hands. This is especially noticeable upon shaking hands with another member of the family, when neither can let go.

I observed him after having had a slight operation on his nose, under cocaine. He arose from the chair, thus bringing his feet into plantar flexion. They remained in this position, and it was necessary for him to walk on his toes for several steps. At this same time the

myotonia of his hands was especially marked. The von Graefe sign, though present, is not so salient as in other members of the family. His mother, however, states that she noticed it first when he was an infant. On examination he was a thin, dark, active, intelligent young man. The examination of the chest, abdomen, skin, and lymphatics was without especial findings. Myotonia of the upper and lower extremities was marked while under examination. The von Graefe sign was not then present. Mechanical stimulation of the muscles by tapping, gave a markedly slow reaction. In addition, I have observed T, M, and A, of the fourth generation, none of whom show any myotonia. Ar and Heb, of the fifth generation, daughters of Ha, both show the von Graefe sign. Heb was three years old in November, 1909. She was a breast-fed child, and has been well except for frequent attacks of rhinitis. She is well nourished, and, with the exception of adenoids, gives no general physical findings of interest. It was possible to demonstrate a contraction of the interossei with 1.5 milliamperes, and no difference could be made out between the AC and the CC contractions. Faradic stimulation gave a marked reaction.

Ar was six years old on November 17, 1909. She was a breast-fed child, and with the exception of diarrhœa at the age of three months, and tonsillitis last winter, has had no acute affections. Her mother noticed the von Graefe sign when she was six weeks old. No other manifestation of the myotonia has been noted by the family. She is a well-nourished child, with no evidence of myotonia in her voluntary motions except the von Graefe sign. This is, however, not so marked as with her father, Ha. The pupils react normally to light and accommodation. The cervical lymphatics are palpable and the tonsils enlarged. The examination of the chest and abdomen shows nothing abnormal. The patellar, Achilles, and cubital reflexes are present. Faradic stimulation of the muscles gives a reaction with a much weaker current than is the case with her non-myotonic brother. The contraction is slow and lasting. Galvanic stimulation of the interossei gives a reaction with 2 milliamperes, and the ACC equals the CCC.

That so well-known a sign should be the salient feature of this familial condition is evidently rare. If we except the single case of Oppenheim, in which there is no record that the von Graefe sign is characteristic of the myotonics of a whole family, it is probably unique.

TORSION OF THE GREAT OMENTUM.

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It is only in recent years that the great omentum has come into much prominence in surgery and medicine. What its functions are is difficult for us to realize, since they are so numerous. The great omentum begins to develop in the third month. It starts at the greater curvature of the stomach and, extending gradually downward, passes over, first, the transverse colon and the small intestines. As it comes in contact in the first part of its course with the transverse mesocolon, the great omentum fuses with this and with the transverse colon, and their relations become permanent. The great omentum, or mesogastrium, in its development upward, becomes adherent to the ventral surface of the left kidney, so that it is adherent to the parietal peritoneum of the left kidney. Perhaps a small part of the omentum, in its development downward, becomes adherent to the parietal peritoneum of the right kidney, since the mesocolon, becoming adherent to the primary parietal peritoneum of the right kidney, leaves a surface with which the great omentum could easily fuse, just as its dorsal layer fuses with the transverse mesocolon. Or this condition of adhesions of the great omentum to the right kidney may be due to the fact that the ascending mesocolon does not adhere to the primary peritoneum of the right kidney, so that the great omentum attaches itself to the primary peritoneum, and then continuing its development causes a torsion of itself; or the great omentum becomes adherent to the parietal peritoneum of the right kidney before the ascending mesocolon becomes adherent to it. Any one of the above conditions could easily occur and no symptoms manifest themselves until some inflammation sets in in some other organ or organs of the abdominal cavity.

The great omentum, as in the case herewith reported, may give rise to symptoms of disease of other organs sufficient to demand operation, with few symptoms pointing to itself.

On January 19, 1909, Joseph F., aged forty-two years, white, a locomotive engineer, was referred to Dr. J. D. Griffith, at St. Joseph's Hospital. His family history is negative. He has had all the diseases of childhood, and denied venereal infection. About two months before entrance to the hospital, he noticed a slight aching in his right side when he leaned toward that side or against the cab window; the pain was just between the crest of the ilium and the lower border of the rib. About one week before entrance he began to feel extremely sore in the right side, with pain radiating toward the back; and some pain in the stomach, with nausea and loss of appetite. Being strong and healthy, he returned to work, but

again had to quit. A doctor told him his gut was clogged and advised him to take castor oil. This opened his bowels well; the pain over the right inguinal region at the so-called McBurney point increased.

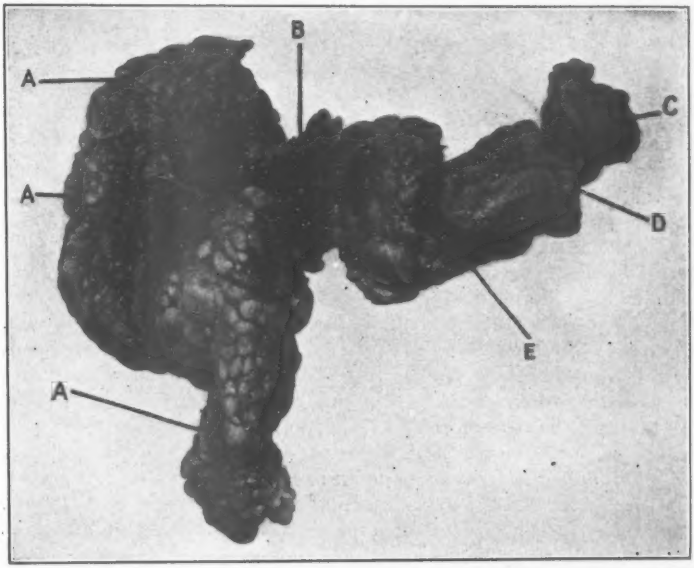
Dr. O'Conner, to whom I am indebted for the privilege of reporting the case, was consulted, and the patient was advised to see his surgeon at once. On examination, there was pain and tenderness over the appendix region, but no tumor was palpable. The right kidney was slightly tender, but no tumor mass could be felt here. The abdominal reflexes were normal. There was no pitting over the anterior superior spine of the ilium, so often found in purulent appendicitis. His temperature on entrance was 99.4°, his pulse 80. There was a slight leukocytosis. The urine was amber in color, the reaction acid; it had a specific gravity of 1020; the daily amount 1500 c.c.; albumin, sugar, bile, and blood were absent. Indican was slightly increased.

A diagnosis of appendicitis was made. The next morning I found that the patient had had a bad night, the pains had increased, his temperature was 100° and the pulse 98. An operation was thought advisable. Under ether anesthesia, an oblique incision about three inches long was made over the appendix region. On introducing the fingers the cecum with the appendix was found adherent to the posterior abdominal wall. After the adhesions had been broken up, a large inflamed appendix was removed. The stump was inverted with a purse string suture after the appendix was ligated off. On returning the cecum and attempting to bring down the great omentum, this was found to be adherent over and behind the cecum or ascending colon. The incision was made larger and the great omentum brought up into view. The point of adhesion was found to be just over the right kidney, the omentum was here twisted on itself, the bloodvessels greatly engorged, and the part at the point of adhesion—the side and not the lower free border—was dark and gangrenous. The adhesions were broken up and the peritoneum sutured over the raw surface. The constricted part of the omentum was ligated off and removed. The accompanying photograph shows the amount removed and the tortuous condition of the great omentum. The omentum was then pulled down and the wound closed. The patient made an uninterrupted recovery.

I have already stated that the patient gave no symptoms of this condition of the omentum, but he did. He complained of pain in the right lumbar region, which increased when he leaned against the window of his cab, or toward that side. However, we often find this is the case in appendicular trouble, and for that reason not enough weight was laid on this symptom.

I found the great omentum covering the ascending colon, a reason for my believing the condition to be congenital, because, as a rule, we do not find it covering that part of the large gut, unless, as I have

said there has been some severe injury to the part; he gave no such history, nor did the gut or kidney region show any signs of injury or inflammatory process. Another very peculiar condition existed: there was no constriction of the gut; it was freely movable under the great omentum, and there was no evidence of bands, which might cause a constriction of the large gut. The soreness in the stomach and vomiting of the patient are explained by the great omentum pulling down on this organ; but the symptoms aided us little in diagnosticating torsion of the great omentum, as this condition is also found in appendicitis. I might say, then, that the pain in the



The points *A A A*, indicate where the specimen was severed from the side of the great omentum; *B*, the point of greatest constriction wherein were dilated vessels and fibrous tissue; *C*, the part that was attached to the peritoneum covering the right kidney; *D*, the gangrenous portions of the specimen; *E*, the twisted condition of the portion of the omentum from *B* to *E*.

right lumbar region radiating to the front and increased on pressure might lead us to diagnosticate this condition, but these are also found when we have trouble in the kidney. I believe, therefore, that we are unable at present to make a positive diagnosis of this very interesting condition until we open the abdomen, and I believe it is often overlooked.

W. W. Grant, of Denver, in 1908, reported a great number of cases of strangulation of the great omentum from pressure or adhesions. I have had four cases, but they were different from the condi-

tions found in the case reported. I agree with Dr. Grant that the condition does not constitute torsion and should not be classified as such. Grant's cases differ from mine in that he could withdraw the mass with intestine from the abdomen. In my case the omentum was firmly adherent to the peritoneum covering the right kidney and had to be gently dissected off. In his case, as in practically every case reported, it was at the lower free end of the great omentum where the torsion occurred. In my case, it was one side of the great omentum, the free edge being free in the abdominal cavity. His case also gives a history of a hernia at one time, which may have been the cause of setting up some inflammation of the gut, in consequence of which the great omentum became adherent without giving any symptoms. Richardson,[1] of Los Angeles, gives a very through description of torsion of the great omentum with a very good classification and definition of the condition. In the case reported the torsion was evidently acute and due to a hernia, as a result of an operation. He states "that the true torsion of the omentum should include only those cases in which twisting of the omentum on itself has caused a sufficient obstruction of the circulation to produce evidences of strangulation, excluding those cases where we have a matting of the omentum into a mass or ball, which produces torsion, also excluding cases where there is strangulation from any other causes than twisting of the omentum." Many cases of so-called torsion of the omentum do not fulfil this definition. Richardson's classification into acute and chronic cases is very good, but I think that the chronic cases are not of secondary interest, because they often seem, at some time, to give rise to acute symptoms. In my case the patient had had mild symptoms for some time; suddenly the symptoms became acute; in fact, so acute that a diagnosis of acute appendicitis was made and operation advised. As stated, the appendix inflammation, starting a general peritonitis (mild), may have caused an acute engorgement of the vessels of the great omentum, which gave the symptoms spoken of; but the great omentum at the point of adhesion below the point of twisting and constriction was gangrenous with very dilated vessels above. I am, therefore, inclined to think that the chronic cases are quite important.

Richardson's discussion of the etiology and mechanism is very clear, but in his case a hernia existed; in the cases reported by Corner and Pinches there seems to be some doubt as to the existence of a hernia, but in my case there was no hernia. There was no tumor to cause a matting or balling; the peritoneum, however, was slightly thickened, yet no reason for this could be found, and it may have been due to the adhesions of the great omentum.

[1] Jour. Amer. Med. Assoc., May 17, 1907.

THE THEORETICAL CONSIDERATION OF THE WASSERMANN REACTION AND ITS PRACTICAL APPLICATION.

BASED UPON A STUDY OF 2750 CASES.

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The reactions based upon the Bordet and Gengou phenomenon applied to syphilis by Wassermann and modified by many others depends upon two factors: (1) The syphilitic serum is said to possess the power of binding or deviating complement when brought in contact with the antigen. (2) The hemolytic system, consisting of any blood corpuscles plus their hemolytic amboceptor—added subsequently or rather after the deviation of the complement is more or less complete—gives no hemolysis.

The Bordet-Gengou reaction is perfectly in accord with the principles of Ehrlich, and in every respect fits the laws of the side-chain theory. Although ingeniously applied, the Wassermann reaction in its first stage, where the complement is presumably bound by a specific antibody and its antigen, in no particular fits the principles of the receptor theory; nor is it at all as specific as the phenomenon that inspired Wassermann to apply it to syphilitic sera. This view of the reaction forces itself upon the worker very early, especially while preparing his extract from non-specific organs.

As is well known, typhoid serum plus bacillus typhosus will bind complement. It is perfectly just to surmise that a syphilitic serum plus the syphilitic incitor will also bind complement. Wassermann thought that in the absence of culturable organisms extracts from the livers of syphilitic fœtuses will admirably fulfil all the functions of a specific antigen. When tried in the actual test, this really proved of great efficiency. A few years later its specificity was fundamentally shaken, for investigators found that sera undoubtedly non-syphilitic were capable of binding complement when brought in contact with the extracts from syphilitic livers. It was also shown that extracts from non-syphilitic organs, and substances whose composition does not in the least justify the appellation of antigen, were capable of deviating complement when brought in contact with specific sera. We have here, therefore, sufficient ground to argue the non-existence of antigenic properties in the inhibitory extracts used and the absence of specific amboceptors or antibodies in the complement-binding reaction according to Wassermann.

Absence of True Antigenic Properties. As is well known, an antigen is a body which when introduced into the circulation of

a susceptible organism is capable of stimulating that organism in a specific manner, with the production in the serum of the said animal of demonstrable specific substances, known as antibodies.

Does the so-called antigen used in the Wassermann reaction fulfil the above requirement? To my knowledge, not in the least. In order to explain the action of the so-called antigen, we will have to go back to its standardization. One unit of antigen is the accepted dose. Its size is established by using a syphilitic series of tubes, each receiving, say, from 0.025 c.c. up to 0.2 c.c. of the given antigen dilution, as the case may be; and the same procedure is carried out with a normal serum. The tubes are incubated at 37° plus 0.1 c.c. complement, and at the end of one hour the contents are tested for the presence of available complement by introducing cells plus their amboceptor. At the end of this time most, if not all, of the normal tubes will have hemolyzed. Not so with the syphilitic serum. Here we may note that the tubes containing the smallest amount of inhibitory extract may have hemolyzed, while those containing a larger quantity are more and more opaque as the highest quantity is reached. One may use a series up to 0.5 c.c. and even more. The dose can be made so large that it will prevent hemolysis even with normal sera. We learn from this that the usefulness of the so-called antigen depends upon the property of preventing hemolysis with sera and also upon the precision with which the dose of one unit is established. Its specificity as regards the production of antibody can be entirely dismissed, for it is highly improbable that the inhibitory extract capable of binding complement with luetic sera should also find analogous substances in the sera of scarlet, lepra, trypanosomiasis and scleroderma sufferers. The reaction is not a specific one, and needs thorough investigation as to its modus operandi. It seems to me that in the sera of the above-mentioned diseases substances develop which are capable of increasing the inhibitory powers of the extract and thus enhance its antihemolytic properties. The manner in which this is accomplished is only a matter of conjecture. It cannot be denied, however, that antibody formation does take place after the implantation of the syphilitic incitor, but that this true luetic antibody has very little to do with the deviation of complement. In order to give a satisfactory explanation as to the manner in which fixation takes place—bearing in mind the various diseases capable of giving a positive reaction—one must take for granted that in syphilis, as well as in other diseases in no way related to syphilis, other substances are formed besides the specific antibody. These other substances are capable, when brought in contact with the so-called antigen, of liberating a third substance from it, which neutralizes, deviates, and inhibits complementary functions. The formation of these other bodies

is constant in syphilis and in leprosy, and may also form in various other diseases, but less uniformly. We have here a logical deduction based on various well-established facts not conflicting with any of the phenomena of complement inhibition, but specially minimizing its specificity. The only true antibody, antigen factor in the test is contained in the hemolytic system, namely, the antisheep or antihuman amboceptor, sheep or human corpuscles.

The various extracts used as antigens contain the substance which is rendered active only subsequent to the addition of serum carrying the necessary quantity of bodies resulting from an infection by certain germs—these bodies, however, not representing the true antibody. Lately, one of the German workers injected luetic extract into a rabbit and could not demonstrate even a trace of antibody in its serum. It may be that the rabbit is not susceptible to such injection. It is also a known fact that those who worked with extracts from luetic fœtal livers—sucking up into the mouth some of the antigen—would not react in any way. I and those who worked with me had the accident more than once without any bad effects. Again, if we should hold responsible a true luetic antibody for the deviation of complement, we must also allow its presence in the sera from all leprosy and trypanosomiasis patients, as well as in some other truly non-luetic conditions. We would also have to ascribe to the extract the power of producing luetic antibody. Neither requirement is fulfilled in the Wassermann test, therefore we are obliged to look for other factors which would in a less conflicting manner answer most or all of the problems evolved. The possibility of the presence of other bodies in the serum of the clinical states mentioned seems to me rational and most likely the true state of affairs. From the number (2930) of analyses carried out in the Montefiore Home Laboratory, I believe that a syphilitic infection—after subsidence of acute manifestations and its gradation into secondary or tertiary stages—produces changes in various organs, preëminently the liver and heart; that these organs, primarily affected by the syphilitic virus or antigen, ever after this serve as depots of the antigen, of course in a much modified form. These organs furnish the true luetic antibody, in accordance with Ehrlich's theory, as well as other bodies of an unknown chemical and biological nature. These depots are differently affected by the syphilitic virus, depending upon the patient's constitution. The stronger the individual resistance and the milder the infection the sooner do the manifestations disappear and the quicker does the reaction become negative after appropriate treatment. Mercury in proper dosage does away with the reaction as well as most of the symptoms. It may be that the antigen depots are affected by the treatment so that no more are furnished to the serum capable of liberating the inhibitory principle from the antigen used, or, that

the mercury neutralizes the various antibodies formed and renders them inert for complement. The following chartered tests will shed some light on the question. The effect of normal sera, as well as sera from syphilitic patients treated with mercury upon strongly positive serum is as follows: When 0.05 c.c. of a positive serum is mixed with 0.1, 0.2, 0.3, and 0.4 c.c. of a normal serum, the reaction remains positive. The same experiment with a syphilitic serum from a patient moderately treated with mercury also gives no change in the positiveness of the reaction when added to 0.05 c.c. of the positive serum.

TABLE I.—EFFECT UPON THE WASSERMANN REACTION WHEN A NORMAL SERUM IS ADDED TO A SYPHILITIC SERUM.

Normal serum.	*Luetic serum.*			*Hemolysis.*
0.1 c.c.	0.05 c.c.	Incubate at 37° for	Remaining technique	None.
0.2 c.c.	0.05 c.c.	20 minutes.	as in Wassermann	None.
0.3 c.c.	0.05 c.c.			None.
0.4 c.c.	0.05 c.c.			None.
0.5 c.c.	0.05 c.c.			None.

TABLE II.—RESULT WHEN A NEGATIVELY REACTING SERUM FROM A MODERATELY MERCURIALIZED LUETIC SUBJECT IS ADDED TO A POSITIVE SERUM.

Hg. luetic serum.	*Luetic serum.*			*Hemolysis.*
0.1 c.c.	0.05 c.c.	Incubate at 37° for	Remaining technique	None.
0.2 c.c.	0.05 c.c.	20 minutes.	as in Wassermann	None.
0.3 c.c.	0.05 c.c.			None.
0.4 c.c.	0.05 c.c.			None.
0.5 c.c.	0.05 c.c.			None.

These experiments, which are still in progress, suggested themselves when the raison d'être of the disappearance of the positive reaction after mercury exhibition was considered. Another series of experiments were performed to note the effect upon the positive serum from a negative individual who received a few hypodermic injections of mercury This serum, when brought in contact with 0.05 c.c. of a positive serum in doses ranging from 0.1 to 0.5 c.c., was capable of changing the reaction from positive to negative. The experiments show us that in certain doses a normal serum, as well as a negative syphilitic serum, is not capable of doing away with the positive reaction of another syphilitic serum, whereas a normal serum treated with mercury is fully capable of doing this as shown by the charted experiment.

TABLE III.—THE WASSERMANN REACTION WHEN SERUM FROM A MERCURIALIZED NON-LUETIC PATIENT IS ADDED TO A POSITIVE SERUM.

Hg. normal serum.	*Luetic serum.*			*Hemolysis.*
0.1 c.c.	0.05 c.c.	Incubate at 37° for	Remaining technique	Slight.
0.2 c.c.	0.05 c.c.	20 minutes.	as in Wassermann	Complete.
0.3 c.c.	0.05 c.c.			Complete.
0.4 c.c.	0.05 c.c.			Complete.
0.5 c.c.	0.05 c.c.			Complete.

These facts give us many chances for speculation. We must admit that in the given dose a normal serum cannot make a positive serum negative, because there is nothing in this serum directly to injure the red cells used, nor is there present a substance capable of doing away with the body in the positive serum partly responsible for the complement fixation. The case is quite different with the normal serum treated with mercury. In this serum it is evident that a molecule is present which is capable of either injuring the red cells directly or interfering with the property of the inhibitory body in the positive serum. Whether the red cells are injured by the addition of the normal serum treated with mercury, or the inhibitory body in the positive serum was crippled by the addition, is not entirely settled. It is, however, not erroneous to argue that whereas the syphilitic serum treated with mercury was not capable of doing the same as the normal serum treated with mercury; that in the former the mercury was bound to the bodies responsible for the inhibition, rendering these bodies inert so far as deviation of complement is concerned; and that in the normal serum the mercury was not bound, and therefore capable of uniting with the inhibitory body of the subsequently added positive serum and rendering it negative. The difference between the mercury in a normal serum and in a negative syphilitic serum lies in the fact that in the former the mercury is free, there being no positively chemotactic substances to bind it, whereas in the latter it is more or less firmly held by the products of the luetic antigen. The union, if there is one, is firm enough to render the mercury harmless when added to a positive is specific serum, contrary to the conditions that prevail when a mercurialized normal serum is added. A practical application of the above tests will be advanced later. Another interesting phenomenon was observed when we worked with sera containing bile products. All such sera (18 in number) gave a positive Wassermann reaction, although in most of them syphilis could be absolutely excluded. We, therefore, thought that bile or one of its constituents may have something to do, directly or indirectly, with the positive reaction. In fact, bile added to normal serum will make it react positively. The doses of bile added ranged from 0.01 to 0.05 c.c.

TABLE IV.—EFFECT UPON THE REACTION WHEN A BILE SUSPENSION IS ADDED TO A NORMAL SERUM.

1 per cent. bile susp.	*Normal serum.*			*Hemolysis.*
1 c.c.	0.2 c.c.	Incubate at 37° for	Remaining technique	Slight.
2 c.c.	0.2 c.c.	20 minutes.	as in Wassermann	None.
3 c.c.	0.2 c.c.			None.
4 c.c.	0.2 c.c.			None.
5 c.c.	0.2 c.c.			None.

Whatever these results suggest, they are at best speculative, and only future work on a greater scale will enable us to handle this

subject with a more palpable knowledge of the phenomena at the bottom of the reaction. At present, we possess very few facts as to the real value of the reaction, hence the disappointment experienced by many who expected to find in the test the solution of many an obscure clinical problem.

The majority of sera submitted for investigation and analysis are for diagnostic purposes. The question asked, is the serum from a patient with syphilis or not? Bearing in mind the facts stated before, I believe it is not just or safe to render a decision either one way or the other. It must be remembered that in the absence of bile in the serum—and if one can exclude the various clinical conditions before mentioned—a positive reaction certainly means syphilis. A very important fact must also not be forgotten, and that is, that certain luetic sera give a negative reaction; therefore a negative result for diagnostic purposes is valueless and for the reason above stated. This was known from the very earliest, when the test was carried out in but a few laboratories abroad. The serologist, nevertheless, is often reproached for rendering a negative report in just such cases. I therefore advise to send sera for diagnosis only when the clinical findings are extremely obscure, and even in such a case only a positive reaction is of help; a negative reaction leaves the clinician in the same quandary as before. Knowing the shortcomings of the test, the doctor in such a case must form his own conclusion, or give the patient the benefit of the doubt and treat him for lues—unless time is a factor and more urgent interference is necessary. This is especially true in surgical conditions of the brain and spinal cord. I believe that, whenever time permits—in other words, when alarming symptoms do not urge an operation—the patient is to be thoroughly mercurialized and the least improvement noted. If no improvement is apparent—plus a previous negative reaction—the underlying cause is likely not syphilis, and operative interference is justifiable. Surgical skill is also to be resorted to when the reaction is positive in cases in which the syphilitic deposit is accessible with safety and without injury to neighboring tissues, but it is advisable to exhibit mercury first even in such cases.

The diagnosis of syphilis under certain conditions is circumstantially a matter of some difficulty from the initial lesion to tertiary or late manifestations. I do not include signs that are incontrovertible; I refer here only to symptoms and appearances that are confusing. Sera from such patients are to be submitted—with a thorough history of previous treatment—to exclude the neutralizing effect of mercury, the iodides, or arsenic. Compound cathartic pills, if taken regularly, will make a serum negative. It is not fair to send a serum from a treated patient for diagnosis and not acquaint the serologist with these facts. Such sera from treated patients are to be designated, test serum for therapeutic

efficiency. The results obtained by the serologist and the report submitted with such a knowledge is of greater help to the doctor, as under such conditions, from previous experiences, the laboratory worker can better guide the therapeutist as to the dosage to be employed in overcoming the symptoms, or eliminating the reaction from the serum. Having on a previous occasion determined the positiveness of a certain serum, a negative reaction after a course of treatment is of great help to the clinician, and it may be stated that even in such a case a negative reaction, although desirable, does not always go with the cure of the condition. First, the patient may have another disease antedating the syphilitic infection, or the serum became negative before all of the subjective and objective signs have disappeared. Whatever the case may be, care must be exercised. It is not at all impossible for a glioma to be quiescent for a certain period of time, due to its location or its size, permitting the host to be more or less active. It is also possible for such an individual to contract syphilis. The glioma will continue to grow, produce symptoms; subsequently its location is ascertained, but the serum, nevertheless, gives a positive reaction. After a course of treatment, the reaction becomes negative, but the tumor symptoms still persist. An operation reveals the true nature of the growth, trying the ability of the serologist. It is very plain that in such a case the laboratory expert is not to be blamed, and that a patient may have had in an incipient stage a more fatal disease than syphilis.

It happens often that a doctor wishes to know the reaction of a certain serum in the course of treatment before the patient is discharged. It has been my experience that such curiosity is unwarranted and not to be practised. A serum reaction, after proper therapeutic measures, is of value only when all subjective and objective signs have disappeared, and not sooner. A negative reaction is very often obtained much sooner than a complete cure, and only serves to confuse the clinician. When the patient is clinically well it is time to perform the test. If the reaction is negative, he may be considered well and discharged with instructions to return in three months and have his serum tested. This is to be repeated, and the reappearance of the reaction, even in a mild degree, is to be followed by appropriate therapeutic measures. It has been the custom to be satisfied when the patient's serum reacted negatively with a mild improvement in the clinical signs. This again makes me bring out the contention that the bedside and not the laboratory is the proper place for making diagnoses as well as pronouncing cures. A negative Wassermann reaction does not signify that the patient is rid of his syphilis, for long before all of the symptoms vanish the reaction may be as above stated. It occurred to me, from a great many tests, that there are numerous gradations from a weakly positive to a decidedly negative reaction.

As shown in Table III, the serum may become negative after a few weeks of appropriate treatment. The patient was by no means cured. His serum added to another positive serum did not behave like the serum from the patient in Table II. I advised to push the treatment until a result as in Table II could be obtained. This actually occurred a short time ago, and his serum was not only negative, but when added to another positive serum behaved as in Table IV; in other words, exactly like a normal serum.

TABLE V.—RESULT WHEN A NEGATIVELY REACTING SERUM FROM A THOROUGHLY MERCURIALIZED LUETIC SUBJECT IS ADDED TO A POSITIVE SERUM.

Hg. luetic serum.	*Luetic serum.*			*Hemolysis.*
0.1 c.c.	0.05 c.c.	Incubator at 37° for 20 minutes.	Remaining technique as in Wassermann	Complete.
0.2 c.c.	0.05 c.c.			Complete.
0.3 c.c.	0.05 c.c.			Complete.
0.4 c.c.	0.05 c.c.			Complete.
0.5 c.c.	0.05 c.c.			Complete.

I advise the performance of such a test in every case submitted for therapeutic efficiency, for it appears to me logically as well as from observation worthy of trial.

Before closing, I wish to draw the attention of those who are actually engaged in performing tests with the Wassermann and Noguchi systems. Although older and better known, I personally feel that the system recommended by Dr. Noguchi appears much earlier as an indicator of syphilis than that championed by the Wassermann school. The reaction is a little oversensitive, but when carried out with proper knowledge of the technique the percentage of error in my hands was 2 per cent. or less. The Wassermann test showed at best 7 per cent. of negative reactions in well-authenticated luetic conditions. The Noguchi system can also be utilized to a greater advantage therapeutically. Having obtained, on a previous occasion, a positive reaction with this method, it persists much longer after treatment, sometimes remaining positive for weeks after the Wassermann reaction becomes negative. It also rarely gives a positive reaction with sera from jaundiced individuals. Its simplicity, as well as the mode of keeping the biological reagents, makes it a desirable addition to the serological methods.

I had the opportunity to observe and compare the appearance and disappearance of the Wassermann and Noguchi reactions in four cases of very early chancres, and found an average as the appended table shows:

TABLE VI.—WASSERMANN SYSTEM.

Sore noted from 5 to 10 days.	*3 weeks chancre no therapy.*	*Treated for 10 days rubbing.*	*Treated for 4 weeks rubbing.*
3 cases, reaction negative; 1 positive	All positive	2 negative 1 weakly positive 1 positive	All negative.

NOGUCHI SYSTEM.

Sore noted from 5 to 10 days.	*3 weeks chancre no therapy.*	*Treated for 10 days rubbing.*	*Treated for 4 weeks rubbing.*
3 cases positive	All positive	3 positive	1 positive.
1 case weak reaction		1 weakly positive	2 weakly positive.
			1 negative.

The above tends to point toward a greater sensitiveness of the system introduced by Noguchi, and in my opinion is very good for therapeutic uses. When used alone, I believe one can depend upon the results obtained by less-advanced workers, provided the laboratory report is used as a therapeutic guide. For diagnosis, I prefer the use of both systems, repeated twice.

My conclusions derived from the foregoing data are as follows:

1. Not only syphilis, but many other conditions give a positive Wassermann reaction.
2. It is not, strictly speaking, specific for syphilis.
3. It is also not specific in the sense of Ehrlich.
4. For diagnostic purposes a negative reaction is of value only when the patient shows signs resembling an initial lesion, or symptoms bordering on this period.
5. In my experience neither the Wassermann nor the Noguchi systems alone are sufficiently accurate for diagnostic purposes. Both systems are to be used.
6. Having excluded the conditions mentioned in the beginning of this paper, a decidedly positive reaction with both methods is highly suggestive of syphilis even if no direct history of an infection is obtainable.
7. It is of no value to perform the test on sera without acquainting the serologist with the therapy.
8. A negative Wassermann reaction is no indication for cessation of treatment. A much better therapeutic gauge, in my opinion, is the experiment suggested in Table IV.
9. Results from different workers will have to differ until the technique becomes more uniform.

Having been aided in this work by a large number of physicians in the city of New York and its immediate neighborhood, as well as from remote cities, who were kind enough personally to help me to carry out my researches, as well as to supply most of the material, I take this instance to thank them singly and collectively.

My special thanks, however, are due to the visiting staff and resident physicians of the Montefiore Home proper, as well as its board of directors, whose generosity in furnishing the funds necessary for such special work enabled me to carry on the work uninterruptedly.

CALCIUM METABOLISM, WITH SPECIAL REFERENCE TO EXOPHTHALMIC GOITRE.

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In recent years much attention has been paid to the inorganic salts of the body, and many metabolism records of health and disease include estimations of calcium and magnesium and some of sodium and potassium. Besides the consideration of the metabolism phenomena, the pharmacological effect of the minerals and the mineral content of the tissues has been studied. The result of this widespread interest has been the accumulation of a large amount of material. No large work has been inaugurated in this field as was done by the United States Government in the case of nitrogen, and general principles must be deduced from a consideration of all the work collected. Calcium occurs in sufficiently large quantities to make the necessary error of all metabolism work a small percentage of the whole amount, and the process of quantitative estimation is not difficult; hence, the number of calcium records available as compared with those of other minerals is large. The special problems of metabolism, absorption, equilibrium, etc., are as indefinite with reference to calcium as uncorrelated results can make them. For this reason, and because the results of my own experiments can only be interpreted by a comparison with those of others, it seemed necessary to sum up as briefly as possible the work which has been done on these points.

In regard to the degree of absorption there is an insuperable difficulty. Voit[1] found, when he fed an animal on a diet containing a small amount of calcium, that he obtained more calcium in the feces than was contained in the food; he concluded that calcium was excreted by the intestinal wall. The import of this finding was more fully understood when Rey,[2] having cleared the intestinal canal of animals, gave subcutaneous injections of a calcium salt; he learned by this method that the amount excreted by the intestinal wall might reach over 50 per cent. of the intake, but that the variation was great. There remains the consideration of the balance obtained by deducting from the calcium intake the urinary and gross fecal output without reference to the part of this which is used in the body processes. This balance has been found to be affected by the following conditions: (1) Underfeeding or overfeeding with reference to the physiological requirement; (2) starvation; and (3) pathological conditions.

[1] Ztschr. f. Biol., 1880, xvi.

[2] Arch. f. exp. Path. u. Pharm., 1895, xxxv.

The physiological requirement has been estimated variously. Bunge[3] thought that 3.3 grams CaO was necessary each day; Bertram[4] found himself in equilibrium at 0.38 gram CaO for the two days which he followed his metabolism; more recently Renvall[5] did an experiment on himself covering a period of fifteen days; this is the longest and most convincing record of calcium metabolism in a normal person. Taking 0.85 to 0.9 gram CaO a day, Renvall found that there was a daily variable loss or gain in the hundredths of a gram; since he weighed 62 kilograms, this gives 0.014 gram CaO per kilo of body weight each day for an adult.

A large amount of work has been done on underfeeding in animals; since rickets and osteomalacia were the most striking examples of calcium disturbance in human pathology, it was natural that they should be the objective point of experimental work. In 1880 Voit was able to accomplish what others had tried with varying success. He reduced the calcium intake of puppies to its lowest terms, and found that after a period of from one to four months, depending on the size of the breed of dog used, the muscle and fat were normal; but the bones were vascular, porous, fractured and fissured in places, and the teeth were imperfect. His calcium-poor diet contained about 0.05 gram CaO daily, and the normal 0.7 gram CaO each day. Though he thought he had produced rickets experimentally, later work showed that there were important differences between the two conditions; but he did show that in the growing organism the lack of calcium is felt most by the bones. Goitein[6] found the physiological requirement of a rabbit to be 0.16 gram CaO per kilo of body weight daily. He concluded from the results he obtained when he varied this amount that with a calcium-poor diet there was a calcium loss, and with a calcium-rich diet there was a calcium retention. The first half of this conclusion for rabbits has been sustained for human beings in calcium underfeeding by the work of von Wendt.[7] He found that a constant loss of calcium up to 0.1 to 0.2 gram a day accompanied a diet containing 0.05 to 0.1 gram daily. Müller[8] and his colleagues found that the calcium output of a starving man was greater than the calcium content of the drinking water.

The subject of calcium overfeeding has been approached by the following workers: Bertram (1897) took 30 grams of the carbonate; he recovered it partly, unchanged in the feces, which showed white with the grains of the salt contained. Herxheimer[9] (1897) also observed himself, and took the carbonate, 18 grams for five days, and 6 grams for the following three days, in the form of a bread

[3] Albu, Neuberg, Mineralstoffwechsel.
[4] Ztschr. f. Biol., 1878, xiv.
[5] Skand. Archiv f. Phys., 1904, xvi.
[6] Archiv f. d. gesamt. Phys., 1906.
[7] Skand. Archiv f. Phys., 1905.
[8] Ztschr. f. Biol., xx; Virchow's Archiv, 1893, cxxxi.
[9] Berl. klin. Woch., 1897, No. 20.

that was manufactured for metabolism disorders. He found a retention of 15.9 grams CaO in the eight days of the experiment. Kaufmann and Mohr[10] (1903) obtained the calcium balance of two patients in the hospital who had no demonstrable lesion. Milk was given in addition to other things, and the calcium intake in one case was 6 grams CaO and in the other 4.4 grams daily. The former retained 16 grams in seven days and the latter 20 grams CaO in ten days. Renvall (1904), in an experiment on himself, used the carbonate in small doses; after the fifteen days of normal metabolism record, referred to under the physiological requirement, he began with 0.5 gram of the carbonate, and retained steadily and continued to do so when he increased the amount to 1 gram. He reached equilibrium about seventeen days after he began to take the carbonate. Thus, the latter half of Goitein's conclusion is supported by four experiments on human beings; a calcium-rich diet (one containing over 2 grams CaO a day) is followed by a calcium retention.

Before passing to the consideration of pathological conditions, one other point must be mentioned which seems, in the few cases in which it has been tried, to affect the calcium balance. The addition of sodium chloride in any appreciable amount appears to increase the calcium output. This is shown by Marischler's[11] work in nephritis and Moraczewski's[12] in carcinoma. The former followed the metabolism of 7 cases of nephritis for nine days each; he divided the whole time into periods of three days each, and gave 6 grams NaCl daily on the second set of three days. In 5 of the 7 cases there was an immediate drop in the calcium retention, or a small retention was converted into a loss. The latter added 10 grams NaCl to the diet of a patient having carcinoma; the calcium balance became negative, though it had been positive on the same calcium intake before the NaCl administration was begun. He obtained a different result in his case of chlorosis, but the NaCl period here followed the administration of so many other salts that the picture is not clear. The pathological conditions have been studied almost entirely from the standpoint of calcium overfeeding, not so much intentionally as because this is an accompaniment of the milk diet, which is both an easy form of nutrition for metabolism work and indicated in many forms of disease.

Rumpf[13] (1897) obtained the calcium balance of a girl, aged nineteen years, who had a stomach ulcer. She was on a milk diet, and received 3.3 grams CaO a day; she retained 1.8 grams CaO daily.

Moraczewski[14] (1901) found a constant negative balance in a case of diabetes with an intake of 1.6 grams CaO a day in the food.

[10] Berl. klin. Woch., 1903, No. 8.
[11] Archiv f. Verdauungsk., 1901.
[12] Zeit. f. klin. Med., 1898, xxxiv.
[13] Berl. klin. Woch., 1897, No. 13.
[14] Zeit. f. klin. Med., 1897, xxxiii.

He changed this to a positive balance by adding 10 grams of the phosphate of calcium and bringing the whole intake up to 5.3 grams a day; the withdrawal of the phosphate was immediately followed by a loss which was a second time counteracted by administering the phosphate, this time in smaller doses; in five days, with an intake of 2.3 grams daily, there was a retention of 2.15 grams.

Ott[15] (1901) worked with phthisical subjects, and found a positive balance in 7 out of 8 cases.

Hirsler and von Terray[16] (1905) followed a case of endo-arteritis, a male, aged fifty-seven years. They divided a six-day period into two of three days each; they gave milk in the first period and added bone meal in the second; the patient retained 3.9 grams CaO in the first three days and 5.3 grams CaO in the second period.

King[17] (1907) followed the metabolism of a case of arthritis deformans; the Folin diet was used, and found to contain an average of 4.6 grams CaO in a day; in the five days of the experiment there was a retention of 9.6 grams CaO.

A calcium loss was found in diabetes by both Moraczewski and Gerhardt and Schlesinger;[18] in the latter work at least there was a coincident factor, which occurs in other pathological conditions, and has always been found to be accompanied by a calcium loss; that is, acidosis. Besides this work of Gerhardt and Schlesinger's there is the record of a case of acidosis of unknown origin obtained by Barker and Voegtlin;[19] in this case there was a high organic acidity, and the chief output was through the intestine. Falta and Whitney,[20] after the extirpation of the pancreas of a dog, found an increase of the output of the calcium in the urine. The ammonia was not estimated, but the uric acid rose considerably, and a state of acidosis seemed likely, due either to the removal of the pancreas or to a postoperative acidosis. Some work has been done on the administration of acid by the mouth. Rüdel[21] gave dilute hydrochloric acid to a child and obtained an increase of the calcium of the urine; later, he gave concentrated HCl to a dog, and found a still greater increase of the output of CaO. Gaehtgens[22] observed a dog for nine days, and in the second group of three days gave sulphuric acid; the ammonia rose to three times its former value, and the urinary calcium was increased. He quotes Kurtz as having given sulphuric acid and having a general increase in the output of the salts; potassium was the one most affected, but calcium, magnesium, and sodium were all increased. The ratio of the urinary and fecal output of calcium has always been of interest, though it is of limited significance

[15] Deutsch. Archiv f. klin. Med., lxx, and Zeit. f. klin. Med., l.
[16] Zeit. f. klin. Med., 1905, lvii.
[17] Johns Hopkins Hosp. Bull., June-July, 1907.
[18] Arch. f. exp. Path. u. Pharm., xlii. [19] Johns Hopkins Hosp. Bull., June-July, 1907.
[20] Beitr. z. chem. Phys. u. Path., 1908.
[21] Arch. f. exp. Path. u. Pharm., 1894, xxxiii.
[22] Zeit. f. phys. Chem., 1880.

as an indication of the degree of absorption. By arranging the results of the metabolism work in the form of a table, we see that on an intake of 4 to 6 grams CaO daily the fecal output ranges beteeen 85 per cent. and 95 per cent. of the whole output; the exceptions to this are King's case of arthritis and one of the cases of chlorosis in which it was 70 per cent. Renvall showed a high urinary output up to the time he began to take the carbonate; in the first two periods 60 per cent. and 64 per cent. were excreted through the kidneys. In Gerhardt's case of diabetes, in the period in which the acidosis was not combated by the alkali, the urinary output of calcium rose to 73 per cent. of the whole output. There is a certain amount of agreement between the cases on an intake of 1 to 2 grams CaO daily; many of them have approximately 60 per cent. of the output fecal and 40 per cent. urinary. This is, however, by no means universal; all the carcinomas and several of the chlorotic cases differ from it very markedly.

TABLE I.

Author.	Daily intake in grams CaO.	Urinary per cent.	Fecal per cent.	Author.	Daily intake in grams CaO.	Urinary per cent.	Fecal per cent.
Van Wendt	Normal, 0.05	10.0	90.0	Mayer	Phthisis, 1.5	40	60
"	" 0.2	21.0	79.0	"	" 2.0	37	63
Renvall	" 0.85	60.9	39.1	Moraczewski	Carcinoma 10 gms. $Ca_3(PO_4)$	11	89
"	" 0.9	64.3	35.7	"	Carcinoma, 1.3	13	87
"	" 0.9	29.1	70.9	"	" 1.3	6	94
"	" 0.9	36.1	63.9	"	" 1.3	9	91
"	" 0.9	25.4	74.6	"	" 1.3	12	88
Herxheimer	" 11.6	7.5	92.0	"	" 2.9	5	95
"	" 3.7	12.4	87.0	"	" 0.9	71	29
Kaufmann and Mohr	" 6.0	8.0	92.0	"	Chlorosis, + 10 gms. $Ca_3(PO_4)$	29	71
" "	" 4.5	8.0	92.0	"	Chlorosis, + 10 gms. $Ca_3(PO_4)$	11	89
King	Arthritis, 4.5	30.5	69.5	"	Chlorosis, 0.9	20	80
Barker and Voegtlin	Acidosis	14.3	85.7	"	" 1.3	40	60
Gerhardt and Schlesinger	Diabetes, 0.8	38.0	62.0	"	" 0.9	40	60
" "	" 0.8	73.0	26.0	"	" 0.9	40	60
" "	" 0.8	55.0	45.0	"	" 1.4	9	91
Hirsler and v. Terray	Arteriosclerosis, 5.8	6.9	93.1	"	" 1.4	39	61
" "	" 7.2	7.4	92.6	"	" 0.9	9	91
Ott	Phthisis, 4.4	5.0	95.0	"	" 1.4	4	96
"	" 6.1	13.0	87.0	"	" 1.4	9	91
"	" 6.0	6.0	94.0	"	" 1.4	19	81
"	" 4.5	7.0	93.0	Towles	Hysteria, 0.3	40	60
"	" 4.5	6.0	94.0	"	" 1.2	36	64
"	" 2.3	7.0	93.0	"	" 1.2	39	61
"	" 4.0	7.0	93.0	"	" 1.2	28	72
"	" 2.4	6.0	94.0	"	Exophthalmos, 3.8	16	84
Mayer	" 1.5	40.0	60.0	"	" 3.8	10	90

Table I shows the great variation in the ratio of the urinary and fecal calcium output in normal as well as pathological conditions.

A most important contribution to our knowledge of the course of events in calcium metabolism when a sudden and severe drain is made upon the calcium of the body was made by McCallum and Voegtlin[23] in their article on the "Extirpation of the Parathyroid." They found that after this operation dogs developed symptoms of tetany which disappeared when calcium was administered; analyses of the tissues showed that there was a decrease of the calcium content of the soft parts and the blood. Since the bones were not obviously affected the condition was one in which their calcium was not available, probably because the whole process was too acute.

This consideration of the literature allows the following conclusions to be drawn as far as one may conclude anything from records which cover so short a period as many of those quoted do. Absorption is an unapproachable problem. The physiological requirement is about 0.014 gram CaO per kilo daily for an adult. Underfeeding of calcium is followed by a calcium loss. A diet rich in calcium is followed by a calcium retenion. Acidosis is accompanied by a calcium loss.

Since the thyroid gland is so closely associated with metabolism phenomena and cases of exophthalmic goitre were easily obtainable, it seemed advisable to investigate the calcium balance in this condition. The literature of the metabolism of Basedow's disease is given fully in von Noorden's text-book; a considerable number of cases have been followed for the nitrogen metabolism, and the results have been identical; namely, that in most though not all of the cases there is a loss of nitrogen in the later and more severe stages of the disease. No change was found in the chlorides and the phosphates were inconstant, and in no cases had the calcium been determined.

Three weeks was decided upon as the longest time feasible for following the metabolism of a hospital patient; as it was impossible to keep a person on the same diet daily for that length of time, a rotating diet was devised, which contained the same amount of calcium daily, and also as little as possible, that the effect of the calcium salt administered might be evident. The diet consisted of 30 grams of oatmeal weighed raw, 150 grams of bread, 90 grams of butter, 3 grams of salt, 50 grams of sugar, 50 grams of cream, one cup of coffee, 1500 c.c. of water daily; 150 grams of beef, 150 grams of potatoes, 100 grams of spinach; or 150 grams of lamb, 150 grams of rice, 100 grams of peas; or 200 grams of chicken, 150 grams of potatoes, 100 grams of cauliflower on successive days, and repeated in regular order through the weeks of the work.

[23] Jour. Exper. Med., 1909.

At the end of the day, when the residues were weighed out, one-half the quantity actually consumed was weighed for analysis, put through a grinder into an evaporating dish, together with the washings of the grinder itself, and evaporated to dryness on a steam oven and dried at 110° for thirty-six hours, weighed and powdered. The mixture contained six articles daily; the butter was analyzed separately. The same diet was used in both cases. A preliminary period of four days in which no calcium was given preceded the administration of the calcium, which was given in the form of the lactate, and in this first case in doses of 5 grams daily, in capsules. The feces were marked off at the end of four, six, five, and four days, with decalcified charcoal, for the purpose of separating the preliminary period from the rest of the time, and of obtaining the balance at intervals through the calcium taking time. The urine was collected from 7 A.M. to 7 A.M., and all estimations were made on the same day that the material was sent to the laboratory.

The first patient was aged thirty-one years, single, occupied a separate room, and was attended by a special nurse. Physical examination revealed no abnormality, and her difficulty in walking for which she entered the hospital was diagnosticated by Prof. Barker as hysterical, and this was subsequently confirmed by her recovery. Unfortunately she was very constipated, and a plain water enema was given daily; in addition to this a purgative was given once during each period (2 drams of castor oil). Her weight, one hundred and forty-eight pounds, was the same at the end as at the beginning of the experiment. Table II shows the food nitrogen and calcium and the urine and feces; also the total acidity, the phosphates, and the ammonia of the urine. The nitrogen was estimated by the method of Kjeldahl, the ammonia by the Folin method, the phosphates by titration with uranium acetate, the total acidity by titration with one-tenth normal NaOH solution with phenolphthalein as an indicator, the calcium was brought down in a solution of acetic acid as the oxalate and titrated as calcium with potassium permanganate.

An accident to the tray on which the patient's meals were served, on the ninth day of the experiment, makes the intake of that day a little uncertain; but the calcium of the food was so small a part of the whole amount that no great error could have occurred. The preliminary period showed a loss of calcium, the first and second periods of the calcium-taking time a slight retention; the urinary calcium was of a higher daily average than the calcium of the food; in the last period there was a slight loss. The patient had been in the hospital three weeks, and had taken considerable milk in that time, so that the observation follows a period of calcium-rich diet.

TABLE II.

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
Food.																			
Nitrogen	10.31	8.09	9.15	14.35	11.40	13.80	9.66	10.81	10.96	9.25	12.68	15.07	9.65	8.17	13.49	9.21	13.85	12.70	12.81
					0.909	0.909	0.909	0.909	0.909	0.909	0.909	0.909	0.909	0.909	0.909	0.909	0.909	0.909	0.909
Calcium	0.3547	0.2359	0.4192	0.3126	0.2022	0.2299	0.4356	0.2862	0.1145	0.3644	0.2359	0.2337	0.4332	0.2283	0.3648	0.3648	0.2328	0.2268	0.2596
Urine.																			
Quantity	1820 c.c.	1090	1300	970	1240	1070	1052	1100	900	1249	910	1225	1545	710	919	1420	1350	1565	1000
Acidity	473	452	318	300	192	214	115	177	207	124	182	214	123	117	188	142	162	125	220
Ammonia	0.8635	0.982	0.7403	0.6812	1.001	0.7276	0.4471	0.4320	0.5202	0.4352	0.4486	0.5915	0.3939	0.6095	0.4140	0.4586	0.5622	0.385	0.595
Phosphates	2.82	2.25	1.40	0.714	0.995	1.071	1.01	0.907	1.118	1.29	0.930	1.06	1.13	1.17	1.16	1.24	1.09	0.929	9.57
Nitrogen	10.43	14.64	9.35	9.72	8.12	9.73	8.02	6.57	7.75	8.28	7.02	8.37	7.31	7.36	9.69	8.94	9.90	8.76	8.23
Calcium	0.5619	0.4327	0.2534	0.2562	0.3762	0.3802	0.4099	0.3921	0.3301	0.3386	0.4306	0.4127	0.4219	0.3251	0.3818	0.3839	0.3557	0.2706	0.3901
Feces.																			
Nitrogen	5.4138				4.8069						4.0534					5.6501			
Calcium	3.2104				3.7913						3.0528					3.7883			
Quantity	79 grams				90 grams						70 grams					91 grams			
Balances.																			
Nitrogen	—7.6569				+12.5995						+15.2443					+7.0925			
Calcium	—3.392				+ 1.06						+ 1.0762					—0.4695			

Total nitrogen, +27.2792. Total calcium, +1.660 (in calcium-taking period). Total calcium, —1.7315 (in whole time).

The second patient was aged thirty-five years, and weighed 106 pounds; she had a marked case of exophthalmic goitre; there was a large tumor of the thyroid, a pulse rate of 130 to the minute when she entered the hospital, a fine tremor of the fingers, and considerable exophthalmos; there was little sweating; the heart, lungs, and abdomen showed no abnormality; the urine was negative, and the temperature was normal. This patient had also been in the hospital for some time, and had had milk daily. She was given the same diet as the first patient and 20 grams of calcium lactate daily in water flavored with lemon juice. Her pulse rate was 100 to the minute when the work was begun, and no change took place in this; in general, her condition appeared the same; the patient herself thought she was the same, except that an unpleasant sense of constriction had disappeared from about the throat. On the third day of the second period, the first of the calcium taking, the stools of this patient became very green, and remained so through the whole of the time; but were normal as soon as the calcium was stopped. When the time was about half over we learned that the patient was pregnant, in the first weeks. On the two days indicated by a plus sign the urine was partly lost into the feces, so that, though the whole balance is accurate, the ratio of the urinary and fecal output is lost. Subsequently the patient was operated on by Dr. Halsted and made an uninterrupted recovery, and left the hospital much improved. In this case (Table III) the nitrogen balance was positive in the first period by 5.3 grams, in the second period there was a loss of 4.8 grams, and in the third a loss of 11.4 grams, followed by a retention of 3.4 grams; in the whole time a loss of 7 grams and one pound in weight; the patient was hungry most of the time, which she said was usual with her in the early stages of pregnancy. The calcium balance was negative in the first period and showed a retention in the second of 3.7 grams CaO, followed by a loss of 6.6 grams and in the last period a loss of 0.45 gram CaO; there was a total loss of 5.4 grams CaO. That such a loss of calcium is not an inseparable accompaniment of Basedow's disease is shown by the calcium balance of a patient who suffered with a severe case of exophthalmic goitre; she was aged forty years, and was kept on a diet of 1 liter of milk, 150 grams of beef, and 50 grams of bread; there was a retention of nitrogen; the urinary calcium was low, probably because of a renal insufficiency; the observation lasted eight days; the ammonia and total acidity were normal:

CaO intake.	Urine.	Feces.	Total output.	Balance.
24.48 grams	1.0437	17.5	18.54	+7.94

In this case there was a retention of nearly 1 gram a day on a less intake of CaO in the form of milk.

Shown graphically, the nitrogen and calcium curves in the case in which the calcium lactate was used is as in Charts I and II.

TABLE III.

FOOD.

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
Nitrogen	12.72	10.21	13.30	9.74	10.20	12.60	12.65	8.64	15.11	9.47	10.83	12.60	10.93	10.45	12.50	12.56	14.40	13.80	11.33
					3.636	3.636	3.636	3.636	3.636	3.636	3.636	3.636	3.636	3.636	3.636	3.636	3.636	3.636	3.636
Calcium	0.2361	0.3832	0.2520	0.2529	0.2901	0.2500	0.2084	0.3987	0.2934	0.2494	0.3332	0.2282	0.2157	0.3447	0.2455	0.2165	0.3499	0.2487	0.2325

URINE.

Quantity	670	1480	910	770	760	700	520	1330	860	1660	1060	960	1260	1020	865	1060	810	1485	1420
Acidity	323	148	264	269	315	255	187	234	133	192	79	86	163	86	246	276	129	141	
Ammonia	0.6052	...	0.8315	0.8737	0.9011	0.8181	0.8331	0.7743	0.5957	0.986	1.103	0.7711	0.6693	0.7326	0.5531	0.8284	0.8185	1.016	
Phosphates	1.519	...	1.361	1.55	1.27	1.05	0.729	1.26	0.94	1.28	0.93	0.89	1.21	0.88	1.03	1.21	0.82	1.40	
Nitrogen	8.30	5.05	9.75	9.90	10.40	10.68	8.63	12.88	10.26	13.59	14.31	10.14	14.77	10.24	11.01	14.59	10.17	11.75	5.21
Calcium	0.1485	0.1891	0.2563	0.3452	0.4915	0.4856	0.2216	0.7942	0.5391	0.5233	0.4334	0.4448	0.7008	0.3589	0.5638	0.4202	0.5610	0.7065	0.2830

FECES.

Nitrogen	7.6476	6.7468	8.3377	5.9071
Calcium	2.3387	16.6822	23.6549	14.0739
Amount	143 grams	192 grams	215 grams	118 grams

BALANCES.

Nitrogen	+5.3473	—4.8213	—11.4905	+3.459
Calcium	—2.1536	+3.7685	—6.6093	—0.4560

Total nitrogen, —7.5055. Total calcium CaO, —3.2968 (calcium-taking period). Total calcium CaO, —5.4504 (whole time).

From left to right one square represents a day. The base line is equilibrium. In the nitrogen it is about 11 grams; in the calcium, in the preliminary period, it is 0.22 gram and the rest of the time 3.8 grams CaO; in both substances each square above or below the base line is 1 gram. Evidently the second and third

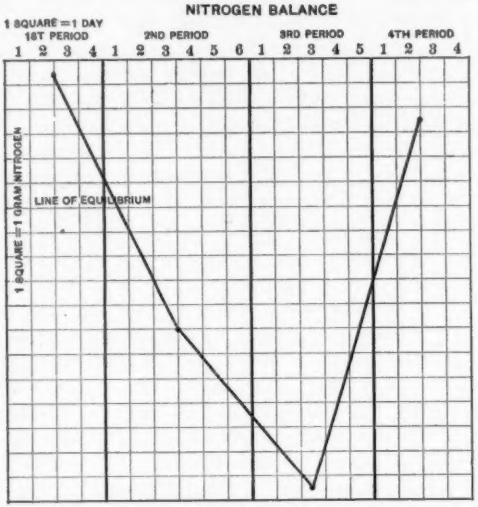
NITROGEN BALANCE
1 SQUARE =1 DAY
1ST PERIOD
2ND PERIOD
3RD PERIOD
4TH PERIOD
1 2 3 4 1 2 3 4 5 6 1 2 3 4 5 1 2 3 4
LINE OF EQUILIBRIUM
1 SQUARE =1 GRAM NITROGEN

CHART I.—Illustrating the nitrogen balance in Case II.

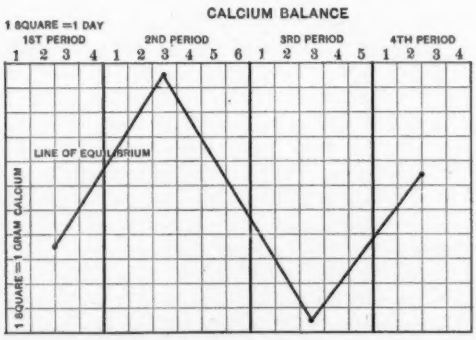
CALCIUM BALANCE
1 SQUARE =1 DAY
1ST PERIOD
2ND PERIOD
3RD PERIOD
4TH PERIOD
1 2 3 4 1 2 3 4 5 6 1 2 3 4 5 1 2 3 4
LINE OF EQUILIBRIUM
1 SQUARE =1 GRAM CALCIUM

CHART II.—Illustrating the calcium balance in Case II.

periods are coincident with such a wave of metabolism activity as others have observed in this disease, or the loss may be associated with the pregnancy.

Whatever may be the cause of the stimulation of the metabolism, the parallelism of the nitrogen and the calcium is apparent. The

loss of the latter substance in the preliminary period is due to the extremely small intake, the usual picture of underfeeding, and that the retention is much smaller than it would be in a normal individual in nitrogen equilibrium I have no doubt; unfortunately both attempts to establish this point were unavailing, since there were losses in the collections that stopped the work. The influence of the amount of calcium taken and the form in which it is ingested upon the retention of calcium and the relation of the nitrogen balance to this may be seen by arranging the results of the work done on calcium overfeeding in the form of a table (Table IV):

TABLE IV.

Author.	Subject.	Form.	Amount. Grams.	Daily Retention in grams.	Retention. Per cent.	N balance in grams.	No. of days.
Herxheimer	Himself	$CaCO_3$	8.0 CaO_3	1.9	23	4.3	8
Kaufmann	Normal	Milk	6.0 "	2.2	38	34.2	7
"	"	"	4.5 "	2.0	47	56.6	10
Rumpf	Ulc. vent.	"	3.3 "	1.8	56		
King	Arthritis	Folin	4.5 "	1.9	41	5.8	5
Hirsler	Arteriosclerosis	Milk	6.5 Ca	1.5	23	14.4	6
Moracsewski	Diabetes	Cal. phos.	5.3 "	1.8	33	2.39	7
"	"	" "	2.3 "	0.4	10	—18.9	5
"	Chlorosis	" "	5.0 "	3.9	78	42.3	5
"	"	" "	5.3 "	4.1	75	24.1	5
"	Carc. vent.	" "	4.3 "	3.1	74	4.3	11
Ott	Phthisis	Milk	4.4 "	0.6	14	0.05	4
"	"	"	6.1 "	0.7	11	—2.39	4
"	"	"	6.0 "	0.1	3	—2.63	4
"	"	"	4.5 "	0.5	11	—3.36	4
"	"	"	4.5 "	0.1	4	—0.08	4
"	"	"	2.3 "	0.1	5	10.0	8
"	"	"	4.0 "	0.2	7	—2.97	3
"	"	"	2.4 "	...	..	0.08	6

The variety of conditions observed and the different amounts and forms of administration used allow but few conclusions to be drawn from this table. It is interesting to note the constancy of the daily retention on an intake of 4 to 6 grams of CaO daily in the form of milk; the agreement of the normal and pathological subjects of observation except diabetes and phthisis; the greater retention of the phosphate; and the parallelism of the nitrogen and calcium balances. It is evident that a loss of calcium may be prevented by a sufficient intake even when there is a large negative balance of nitrogen; this is seen in the second period of the administration of the phosphate in the case of diabetes and in the series of phthisical subjects. That this narrow margin of a positive balance is attained at the price of a considerable diminution of a

possible retention is seen by a comparison with the retention in those cases on the same intake which have a positive nitrogen balance. Recently, Mayer[24] has shown that a positive calcium balance occurred without exception in a series of phthisical subjects on an intake of 1.5 to 2 grams CaO in a day when there was a positive nitrogen balance. Von Wendt showed in a physiological case that with a sufficient though moderate nitrogen intake there was a retention of nitrogen together with a loss of calcium with a calcium underfeeding; also that there was a calcium retention on a moderate intake associated with a nitrogen loss due to nitrogen underfeeding. Renvall had an enormous loss of nitrogen through the whole time of his experiment, and was in calcium equilibrium at an intake of 0.9 gram and retained calcium when he made the small additions of the carbonate. He attributed the loss of nitrogen to the diet he was using, and noted that the fecal nitrogen was unduly high, a condition of underfeeding practically. Thus, we see that while the nitrogen and calcium balances may rise and fall together in a general way, it is a phenomenon of disease rather than of health, and has been found to occur in phthisis, diabetes, and exophthalmic goitre; though even here the calcium balance may be made to be positive with a sufficient intake, though not without evidence of the tendency to loss.

In regard to the cases recorded here, the first experiment shows that the lactate is an easily absorbable salt, as the urinary output is higher than the calcium content of the food. The case of exophthalmos shows a retention of only 15 per cent. of the intake in the first period of the administration of the lactate as compared with 38 per cent. and 40 per cent. retentions in other cases in which milk was used containing approximately the same amount of calcium in terms of CaO, and in which there was also a retention of nitrogen. In the next period, with the loss of 11 grams of nitrogen, there was a loss of 6.6 grams of CaO, while in the case of diabetes there was a slight positive balance, though the intake was 2.3 grams of CaO only and the nitrogen loss was 18 grams. What part of this wide difference is due to the pathological conditions and what to the salts used must be determined by further work.

Conclusions. Calcium given in the form of the lactate enters into the general metabolism or allows the calcium already present in the body to be utilized without loss. Given by the mouth there is no toxic effect from the administration of 20 grams of calcium lactate over a period of fifteen days.

The calcium metabolism of Basedow's disease shows no special peculiarity; it runs parallel with the nitrogen, and in those periods of the disease in which there is a loss of nitrogen there is also a loss of calcium—a parallelism which is found in other pathological conditions.

[24] Deut. Archiv f. klin. Med., 1907.

My thanks are due to Prof. Barker for permission to work in his laboratory and with his patients; to Dr. Voegtlin for the preliminary instruction which made it possible ultimately to undertake this work and his interest and advice throughout; to the nurses in charge of the patients, the Misses Richardson, French, and Allen, and to Miss Wilder, of the diet school, through the long and trying period of the weighing.

HOW FAR IS HEREDITY A CAUSE OF AURAL DISEASE?

By B. Alex. Randall, M.A., M.D.,
CLINICAL PROFESSOR OF OTOLOGY IN THE UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA.

Some five years ago I presented to the Section on Otology of the College of Physicians, but did not publish, a brief note combating the claims made by some authors as to hereditary influences in the causation of ear disease. The subject has considerable practical importance, since we do not wish to waste time upon cases which are foredoomed to afford no success; but also because many people, under an erroneous impression that they are victims of inherited deafness, fail to seek relief at the hands of the surgeon while it is still possible to obtain it. The cure of the chronic catarrhal forms of deafness, not to speak of so-called "otosclerosis," is hard enough at best, and discouragement is all too easy without bringing in imaginary heredity to darken the prospect; yet the claimed bearing of inheritance often seems so far-fetched, if not preposterous, that I again offer a word in opposition,

Just as before I cited two cases of penetration of the drumhead by a twig, and jestingly asked what but heredity had produced this rare accident in cousins, so now it is the close parallelism of conditions in father and son which serves as a text for my remarks. A clergyman came to me nine years ago with Shrapnell perforation and cholesteatoma on the right side and marked defect of hearing from catarrhal deafness on the left. These have yielded none too perfectly to treatment, so that he is still under periodic care, with some tendency to brief recurrence of suppuration in his right antrum, where skin masses collect at intervals until perhaps there is new polyp growth as Nature's protest and effort to expel the collection. Most of the time he is so free from trouble as to be prone to neglect the needed care, while his hearing remains about double what it was on coming, although still imperfect in each ear.

Recently he brought his father because of decrease in hearing, and I found large cholesteatomatous masses protruding from his right antrum and attic, removal of which showed a virtual tympanic exenteration spontaneously done, differing from the

son's only in its greater extent. On the left side there was a depressed drumhead with thin areas, possibly cicatricial, and a stuffy tube, complicated of late by neurasthenic reduction of the acoustic function—conditions almost identical with those found years ago in the son. Eustachian catheterization with dionin has freed his tube, tonic measures have already improved his physique, cleaning up his right tympanum has brought its suppuration to a close, and his hearing on each side seems to be as good as he has known for years.

Heredity is so often dragged in by medical and lay alike in explanation of deafness or the diseases leading to that defect, that it seems only right to meet the claim by renewed query as to how much justification can be adduced for it. Believers in the entity of "otosclerosis" as a *non-sclerotic* disease are apt to cite heredity as one of its most probable factors; and long family trees (of doubtful authenticity to the unenthusiastic mind) are published in support of this contention. Yet it must be conceded by the candid student that the proof of genuine "otosclerosis" is none too positive even in the observed cases, while in most of the unexamined forebears its existence is nearly pure assumption. Deafness marked by exaggerated bone conduction and loss of low tones, with free Eustachian tube, is not necessarily "otosclerosis," even if the drumhead looks normal. The classic definition of amblyopia, in which "the patient perceives a little and the surgeon sees nothing," as sufficiently explaining the defect, ought not to be extended to insidious forms of deafness as diagnostic, especially for the cases which have not even been looked at.

Von Troeltsch told us fifty years ago that one-third of all adults are deaf in one or both ears, and further study has fully confirmed this; and even in the schools 25 per cent. are found deaf. It is a lucky family, therefore, which has not its group of deaf members; and as some families *do* thus escape, there must be an undue proportion in some other families less favorably environed. We could all cite instances of apparent heredity as plausible as those reported; but investigation would quickly prick the bubble in many of them. Those of a family in which four out of five living members showed greater or less deafness a few years ago, were considered by many of their acquaintance as inheriting their deafness. Yet one is a chronic catarrhal case which has advanced little since adult life and permits of some satisfactory hearing at nearly ninety; one an ordnance officer whose defect seemed due to cannonading; one showed defect only about her ninetieth year, with general physical breakdown; and the last has only a trifle of nerve deafness, which interfered little with his usefulness on the bench until his eightieth year, and has not seemed to increase for years. But these are really four children out of eleven, and I can not learn that any of the others showed defect of hearing,

nor that any of their progenitors were deaf, although generally reaching advanced age; and there is no instance of deafness in the younger generation of about a dozen, of whom, however, but two living at over fifty had a deaf parent.

One of my patients, whose condition and history better permit a diagnosis of "otosclerosis" than the majority of the small group which I would so regard, has two sisters also deaf, both with chronic tympanic catarrh in my opinion. On neither side, in the large families behind them, is there known deafness except of one maternal uncle, whose defect did not prevent his serving as an officer through the Civil War, at the close of which he was accidentally killed. I have previously cited this family as an instance of inheritance, for I believe that the children all have the narrow external configuration of the nose of their father, while the internal structures, like those of the larger Roman nose of the maternal side, crowd the nasal cavities and predispose to stenosis and catarrhal troubles. The two brothers have had as much or more nasal affection, but have escaped the ear involvement from which the three sisters have suffered.

A special susceptibility of the mucous membranes seems to be present in some families and to predispose to catarrhal involvement of the nose and ears. Yet it is questionable if this is not largely due to environment except so far as induced by structural configuration, as above indicated, as the sole inheritance. Much more evidence were easily adduced to show that heredity may play an important part anatomically to facilitate or decrease the tendency to ear disease. It is generally recognized that the negro has a wide, straight canal, in which cerumen does not readily collect, while his short, wide Eustachian tube and roomy nose are little prone to catarrhal affections, affording his race a considerable immunity from troubles frequent in the white. Certain families show usually the narrow jaw and high palatal arch which is frequently associated with adenoid hypertrophy of the pharynx vault, and is too often considered a consequence of that condition instead of a cause. I have had to remove wax impactions from the ears of most of the members of one family, all of whom showed a tortuous collapsed canal which must have constituted a predisposition. The straight, open canal of one of my cases of drumhead puncture was surely a factor in facilitating the entrance of the penetrating twig, but it was not present as an inherited feature in his cousin, who similarly suffered.

The assumption of inherited narrowness of the fenestral niches as a factor in fixation of the stapes and round-window membrane lacks confirmatory observations; the claim that spongification of the labyrinth walls has its beginnings in embryonal life is similarly weak; and while Bezold claimed heredity for 52 per cent. of his otosclerosis cases, most students of the matter admit far less, and

Heimann only 9 per cent. A stronger case might really be made for other diseases of the ear, or for those of other organs. Predisposition alone can fairly be claimed as a matter of inheritance in ear disease, and the degree of this is not likely to be agreed upon by the authorities.

The environment, therefore, of those presenting a family history of deafness must receive most sedulous attention, and all habits, such as mouth-breathing, which tend to damage the ears, must be early corrected, by adenoid operation or other intervention if necessary. Careful treatment should be instituted as soon as any defect of hearing is recognized, and pursued thoroughly and hopefully, using the measures which have in careful hands always given fair results, instead of "following after new gods"—often new only to a new generation which does not remember their previous exploding. Heredity must not be assumed as an imaginary bar to the treatment of remediable disease in the ear or elsewhere.

REVIEWS.

URGENT SURGERY. By FELIX LEJARS, Professor Agrégé à la Faculté de Médecine de Paris. First English edition, translated from the sixth French edition. Vol. I; 617 pages; 20 full page plates, 994 illustrations. New York: William Wood & Co., 1910.

THE general plan of this well-known book is more comprehensive than its title seems to indicate. So many operations may be "urgent" that, literally interpreted, as it has been, the title may be made to include perhaps the majority of the operations of surgery. Intraglandular abscess of the breast, abscess in the sheath of the sternomastoid, and a few similar conditions, are but rarely the cause of any real urgency, and might with propriety have been omitted. The work is, however, far more than a manual on "First Aid to the Injured," and is, indeed, a treatise which admirably sets forth the accepted French technique in many important operative procedures. That there is little mention of the differences in detail which would be found on comparison with American or with English methods does not materially lessen its value, and, in fact, by adding to the directness and force of the teachings renders them both more available in a real emergency, and more readable. There have been so many foreign editions of the book—which has been translated into almost every Continental language, including Russian, and into Japanese—that an extended review of this translation does not seem to be needed.

For commendation we would select the descriptions of the management of retropharyngeal abscess in which essential details often omitted are particularized; of the indications and procedure in fractures of the larynx; of the operative technique in wounds of the heart; of the treatment of abdominal wounds, non-penetrating and penetrating; and of the whole clinical series of appendix infections and their complications. The author is always positive in his advice, and in his effort to avoid ambiguity sometimes seems to be a trifle too comprehensive, but careful reading usually shows that he can justify the position he has taken, or that he has made the necessary reservations. For example, his teaching as to appendicitis, while radical to the extent of recommending that "every case of acute appendicitis must be operated on," is conservative in that he would wait, "as often as possible," "until a quiescent stage;" and while

he thinks that in abscess cases the appendix "ought to be looked for," he gives minute directions as to the manner of search, and adds: "Stop in good time if nothing is found; the object of the operation is not to resect the appendix, but to open freely and drain the abscess cavity."

Here and there are statements not in accord with received opinions. It is far from certain that, in fractures of the lower jaw, "when the mouth is opened the posterior fragment is automatically depressed," but the description of the Claude Martin treatment for such fractures —"the open mouth" position—is excellent; and his dictum that the "primary indication" in all these fractures is for "frequently repeated and thorough disinfection of the mouth," deserves emphasis and repetition. So too, while in regard to luxations of the inferior maxilla he mentions only the exploded theory that the obstacle preventing reduction is the engagement of the coronoid process in front of the malar bone, his description of the best method of reduction is unexceptionable.

The translation has been well done. We do not know why the author is a "Professor" agrégé, the rest of his titles being in French. The proofreading has been excellent in spite of a few slips, such as "peritioneal" (p. 499). The illustrations are usually instructive. Fig. 206 (p. 216), "application of a diachylon bandage in a case of fractured ribs," perpetuates a perennial error, the patient being shown with his arms raised so that as soon as they were lowered the most skilfully applied strips would surely loosen. But the same mistake may be found in Scudder, in Keen's *Surgery* (Vol. II), and in various text-books on surgery.

On the whole, the book in its English form is to be welcomed by both practical surgeons and general practitioners. It is to be hoped that the second volume will soon follow, as cross references occur in this one which leave the subject under discussion incomplete, such as the reference on page 118 to "Traumatic Hemorrhage," which is not to be found either in the index or the Table of Contents.

J. W. W.

AMERICAN PRACTICE OF SURGERY. Edited by JOSEPH D. BRYANT, M.D., LL.D., and ALBERT H. BUCK, M.D., of New York City. Vol. VI; pp. 916; 631 illustrations. New York: William Wood & Co., 1909

THE sixth volume of the *American Practice of Surgery* continues Part XVI (Regional Surgery), as follows: Prosthesis in its relation to surgery of the face, mouth, jaws, and nasal and laryngeal cavities, by Charles R. Turner, M.D., D.D.S., of Philadelphia; surgical diseases and wounds of the nasal cavities and accessory sinuses, by

Harris P. Mosher, M.D., of Boston, based on good original work, with numerous valuable illustrations; surgery of the mouth, tongue, and salivary glands, by Geo. E. Armstrong, M.D., of Montreal; of the neck, by John M. Elder, M.D., of Montreal; of the thyroid and thymus, by Francis J. Shepherd, M.D., of Montreal; of the thorax and spinal column, by Norman B. Carson, M.D., of St. Louis; of the female breast, by Harvey G. Mudd, M.D., of St. Louis; of the external genitals and vagina of the female (sic!), by William P. Graves, M.D., of Boston; of the male genital organs, by Franklin G. Balch, M.D., of Boston; chancroid, and gonorrhœal urethritis, by Hugh Cabot, M.D., of Boston, most admirable articles, the latter including the entire subject of strictures; and surgical diseases and wounds of the jaws, by Joseph C. Bloodgood, M.D., of Baltimore.

Among these numerous articles, most of which are of more than average excellence, it is possible to select only a few for extended notice. Turner treats of prosthesis for teeth, cleft palate, and jaws, as well as of artificial noses, lips, ears, tongue, and larynx; no mention is made of the use of paraffin. He urges the use of the prosthesis of Claude Martin, of Lyons, for immediate application after resection of the jaws; though little employed so far in this country, Turner appears firmly convinced of its value.

The most interesting subject discussed by Armstrong is carcinoma of the tongue. He recommends median division of the mandible (formerly known as Sédillot's or as Syme's operation, but lately appropriated by Kocher) only for excision of the entire tongue; for partial excision he uses Whitehead's method; and for cancer of the base or of the lateral posterior aspect of the tongue he prefers Langenbeck's operation. In any case he saws the mandible in a sinuous line, to aid in subsequent coaptation. Perhaps it would have been well if more stress had been laid on bilateral removal of the lymph nodes in all cases. Elder is inclined to conservatism in the treatment of tuberculous cervical lymph nodes. Tumors of the carotid body are not mentioned, though they seem to belong in this article.

Shepherd's article on the thyroid covers nearly fifty pages. He does not tell what the parathyroids are; perhaps this is because he does not know. Certainly, no one else seems to have any clear ideas on the subject; but as he believes that goitre is caused by a microbe yet unknown, it would have been interesing to learn what he thinks of the parathyroids. He discusses *diagnosis* before *symptoms*, and these latter before *classification* or *pathology;* but as the pathology, and therefore the proper treatment, of affections of the thyroid is one of the most difficult problems in surgery today, it is not strange that no thoroughly satisfactory article can be written, but it is rather remarkable that even so experienced and accomplished a surgeon as Shepherd can prepare a monograph open to so few hypercritical objections. He attempts no differential diagnosis of the various forms of goitre, and is satisfied to approve Bloodgood's advice to

remove every asymmetrical enlargement of the thyroid in patients over thirty years of age. He urges the surgeon never to remove the whole thyroid, and always to leave the parathyroids; but in another place (p. 400) he states that he has extirpated completely over a dozen thyroids, and has taken no care to preserve the parathyroids, yet he has never seen a case of tetany except in a patient on whom repeated operations were performed for carcinoma; and at page 392 (footnote) he says that he "is of opinion that, as isolated portions of thyroid never slough when left behind, the parathyroids also get sufficient nourishment from capillaries;" so that he rather minimizes the value of Mayo's and Halsted's recommendation to tie the terminal branches rather than the main trunk of the inferior thyroid artery.

Carson's excellent article on the surgery of the thorax and spine, covering 100 pages, is worthy of careful attention. In speaking of excision of the clavicle for malignant tumors, he questions whether the operation is justifiable in view of the high immediate mortality and the doubtful ultimate outcome. In complete severance of the spinal cord, he advocates its suture, "if only for the purpose of giving the patient a chance to receive that degree of repair which appears to have been granted to others." This is an exceedingly canny statement. He advocates laminectomy for fracture-dislocations of the spine, only after subsidence of shock, in cases in which it is clear that the cord is not irreparably injured. He is very conservative in regard to spina bifida, advising operation only after the age of five years.

Mudd compresses into less than 60 pages one of the most satisfactory accounts of surgery of the female breast which has lately been published. He makes no mention of frozen sections, but speaks encouragingly of the hemolytic test of Crile. He urges beginning the operation by dissection of the axilla. Graves' article on the female external genitalia contains nothing calling for special comment save the number of operative procedures invented by the author. Nearly one-fifth of Balch's article on the male genitals is devoted to anatomy and embryology, though nothing is presented which is not contained in the usual text-books of anatomy. No notice is taken of the teaching of Corner that the imperfectly descended testicle is only very rarely spermatogenetic, and if so, only from twenty to twenty-three years of age; but as the internal secretion is usually quite normal, we fail to understand Balch's advice never to return both testes to the abdomen in children, and cannot approve his preference for orchidectomy when orchidopexy in children is impossible. While excision of such testicles may be quite proper in adults, since the external secretion, if it ever existed, has ceased, and the internal secretion is no longer necessary for physical development; yet surely in children under the age of puberty the testicles should be retained, either inside or outside the abdomen, until male characteristics are acquired.

Bloodgood's article on the surgery of the jaws is illustrated by several excellent colored plates, the delay in the execution of which necessitated placing the text at the end of the volume. He recurs again and again to the idea that no operations, be they ever so extensive, are sufficient for the highly malignant forms of sarcoma, since distant metastases occur very early; and that local, though thorough, extirpations are quite sufficient for the less malignant sarcomatous tumors. The differential diagnosis is to be made by exploratory incision. In the case of carcinoma, on the other hand, distant metastases are almost unknown, and a wide removal of the diseased area and the regionally related lymph nodes, *en bloc*, is the proper surgical treatment. A. P. C. A.

A Text-book of Surgery for Students and Practitioners. By George Emerson Brewer, A.M., M.D., Professor of Clinical Surgery in the College of Physicians and Surgeons, Columbia University, New York. Second edition; pp. 915; 429 illustrations. New York and Philadelphia: Lea & Febiger, 1909.

It is scarcely more difficult for a camel to pass through the eye of a needle than it is for an author to compress the teachings of modern surgery into the limits of a volume moderate in size. In 1903, when Dr. Brewer published the first edition of his excellent text-book (700 pages), he appears to have adopted very radical methods to keep within the limits set for him by the publishers; the latter portions of that volume were therefore less satisfactory than those first written. In the second edition, however, the various parts are well-balanced, most notable additions having been made in the chapters on the head (increased from 43 to 64 pages), the thorax (from 7 to 21 pages), the abdomen (from 68 to 92 pages), the kidneys (from 28 to 44 pages), and the bladder (from 29 to 41 pages). The number of illustrations has also been increased nearly 50 per cent., and several colored reproductions of photographs made by the Lumière process have been added. While the latter are in some ways an interesting addition, it is questionable whether less lurid illustrations might not teach the student quite as much surgery.

While there is little to criticise, and much to praise, in this text-book of Dr. Brewer's, we believe that a little more systematic arrangement of his subject matter would make surgery easier for the student to learn (and this is the main object of any text-book); and that had the principles of surgery been treated a little more fully, space would have been economized and the teaching value of the book increased. The teaching of Dr. Brewer is, above all, sane and safe; he does not run after new gods because they are new, nor does he abandon the old for fear of being thought old-fashioned. He proves all things and holds fast to that which is good. A. P. C. A.

A Handbook of the Diseases of the Nose and Throat. By Eugene S. Yonge, M.D., Physician to the Manchester Hospital for Consumption and Diseases of the Throat, England. Pp. 407; illustrated. Edinburgh and London: Wm. Green & Sons, 1909.

This is an excellent handbook for the instruction and guidance of the commencing specialist, and an admirable handbook, too, for the more experienced one. Clear, concise, accurate, conservative, and resourceful, it commends itself to the reviewer as one of the very best that it has been his fortune to possess. Without any prominent use of the first person singular, it indicates close individual knowledge of the subjects of which it treats, expressed in language so plain as to prevent misconceptions.

The subject matters have been arranged in four sections: Diseases of the nose, the accessory sinuses, and the nasopharynx (why not rhinopharynx?); diseases of the pharynx; diseases of the larynx and morbid conditions of the upper respiratory tract which may occur in the course of chronic or acute infective diseases, and in connection with gout, rheumatism, and certain affections of the skin. This is followed by a modest appendix of formulæ which have been recommended in the text for cleansing or for therapeutic purposes. A sufficiently copious index concludes the volume. Discussion of the first three sections begins with the anatomy and physiology of the structures under consideration, and is followed by a description of the methods of examination. Then anomalies and malformations are recorded, and a systematic study presented of the inflammatory and other diseases and their treatment. The fourth section deals with tuberculosis, lupus, syphilis, leprosy, rhinoscleroma, glanders, acute specific fevers, rheumatism and gout, and cutaneous diseases having analogues in the throat.

The text book is illustrated by fifty-seven plates, many of them beautifully colored to the natural tints, and nothing overdone. Some of the plates contain two or more illustrations. There is an entire absence of any leaning toward instrumentomania, for comparatively few instruments are figured; and of those recommended a large proportion are devices of the earlier specialists.

In describing the anatomy of the structures, allusion is made to its utilization in the differential diagnosis of diseases, and attention is drawn to its significance both in favoring and in hampering surgical interventions. In the latter connection precautionary methods are indicated to prevent untoward results, and these are repronounced in detailing the technique of various operative procedures. The unnecessary or inconsiderate sacrifice of organs or of parts of organs, as, for example, extirpation of the tonsils, and partial or total resection of the turbinate bodies, is deprecated when not absolutely requisite; and while too early recourse to radical operations is disapproved, as in obscure accessory sinus

disease, the mistake of too long continued tentative measures before final resort to radical procedures is deemed equally reprehensible.

In certain surgical interventions usually requiring a minor operation preliminary to the main procedure, intervals of from several days to a fortnight or longer are frequently advised in classes of cases in which other operators allow only much shorter intervals or even none at all. J. S. C.

A Manual of Diseases of the Ear, including Those of the Nose and Throat in Relation to the Ear. By Thomas Barr, M.D., Lecturer on Diseases of the Ear in the Glasgow University, and J. Stoddart Barr, M.B., Ch.B., Assistant to the Lecturer on Diseases of the Ear in the Glasgow University, Scotland. Fourth edition; pp. 477; 3 colored plates and 215 illustrations. Glasgow: James Maclehose & Sons, 1909.

In its present form this manual is one of the best text-books which not only students and general practitioners, but both prospective and practising specialists can consult in studying the pathology and treatment of diseases of the ear, and of such maladies of adjacent structures as are provocative of diseases of the ear. Besides 215 illustrations of anatomy, pathology, instruments for treatment and methods of utilizing those instruments, there are three plates similar to those of Politzer, exhibiting in closely approximative tints the color and general appearance of forty-five representations of the membrana tympani as viewed through the illuminated aural speculum. The textual illustrations, anatomical and pathological, are excellent, with two exceptions where excellence should have predominated; both are pictures of rhinoscopic images, the perspective of which gives a poor and misleading idea of what is really to be seen on inspection by posterior rhinoscopy. We indulge the hope that in subsequent editions these may be changed for pictures in better accord with the good ones.

After an introductory note, six chapters follow on methods of examination, symptomatology, etiology, methods of treatment, operative treatment, and on diseases of the nose and throat in relation to the ear; and fifteen further chapters on the special structures of the ear and the individual diseases in detail, which, with an appendix on otalgia and on nervous and vascular supply of the ear, complete the professional text. Several additional pages record a series of 135 formulæ for the topical and constitutional remedies recommended in the body of the work. Three more pages are devoted to bibliographical references. A very satisfactory general index of 21 pages concludes the volume.

Practically, the complete range of study in connection with dis-

eases of the ear is presented in clear language, without verbosity, in accord with the prevalent views of the best authorities. Even the Bier treatment is alluded to, and while insufficient experience for opinion as to its merits is expressed, the writers add that personally they have gained much relief from all the distressing symptoms of a cold in the head by wearing during the night a broad elastic band lightly stretched around the neck. The instructions as to operative procedures are sufficiently detailed to guide the operator and prepare him for contingencies and sequelæ.

We should like to find in an English text-book some reference to the method of catheterization of the Eustachian tube through the mouth with specially constructed tubes, as published by Ephraim Cutter in this JOURNAL for April, 1872, and which the writer of this review has practised with great satisfaction since that time, guiding the tip of the catheter into the orifice under supervision of the image in the rhinoscopic mirror. It has been commended, too, by Menier, of Paris, Oppolzer, of Vienna, Stanislaus von Stein, of Moscow, and other Europeans, but is practically unknown or unappreciated in Great Britain and in America. J. S. C.

SOURED MILK AND PURE CULTURES OF LACTIC ACID BACILL, IN THE TREATMENT OF DISEASE. By GEORGE HERSCHELLI M.D. (Lond.), F.R.S.M., Late Senior Physician to the Kensington General Hospital and to the National Hospital for Diseases of the Heart. Second edition; pp. 72; 8 illustrations. London: Henry J. Glaisher, Chicago Medical Book Co., 1909.

To those who have heralded the lactic acid bacillus as a panacea and have been led to administer it indiscriminately, Herschell's essay on this subject is heartily recommended. Although evidently himself an enthusiast, he has had the wisdom to emphasize with equal force the dangers and limitations as well as the advantages of soured milk and cultures of lactic acid bacilli as therapeutic agents. The first of the three chapters comprising this little book is a summary of recent advances in the diagnosis of intestinal auto-intoxication. Here he points out the futility of making the tempting diagnosis of auto-intoxication without first proving its existence by appropriate tests for both urine and feces. The second chapter, on the methods of using lactic acid ferments in practice, should prove a disquieting revelation to many who, with little knowledge of the chemistry and bacteriology of milk, have been eager to employ any of the numerous recently exploited commercial lactic acid ferments. Herschell regards as dangerous the use of commercial soured milk and liquid cultures of the Bulgarian bacillus. Dried cultures,

although admittedly the safest and most convenient of the commercial forms of the ferment, he has found for the most part unreliable. He is positive in his opinion that the surest and safest means of introducing the lactic acid bacilli into the intestines is to use fresh cultures of the Bulgarian bacillus, properly prepared in a laboratory, and less than a week old. The diseased conditions in which lactic acid ferments may at times be of value are enumerated in the concluding chapter. The author makes the point that hyperchlorhydria is an absolute contra-indication to all lactic acid therapy. The book is a timely review of a subject, which is attracting much popular as well as scientific interest and concerning which there is much misconception. G. M. P.

La Cure Radicale de la Hernie Inguinal. By Dr. Lucas-Championnière, Honorary Surgeon to the Hôtel-Dieu. Pp. 186; 53 illustrations. G. Steinheil, Paris, 1909.

This volume is the first of a series of monographs which Dr. Lucas-Championnière is preparing on the radical cure of the different varieties of hernia. Based upon the clinical teaching, which the author gave for many years at the Hôtel-Dieu, it is written from the standpoint of the individual surgeon, and plainly sets forth his views and describes in detail the technique of his operation. After a general review of the anatomy of hernia, the problem of radical cure, a criticism of other methods of operating, and an analysis of the results which he himself has obtained, the author proceeds to a consideration of his own method. He maintains that suppression of the hernial contents, ligation of the sac *above* the internal abdominal ring, and overlapping the aponeurosis of the external oblique muscle are essential to the attainment of a successful permanent result. Overlapping of the aponeurosis is stated to be the most distinctive and original element of the operation.

While it will be evident to all who may study this work carefully that it is replete with sound surgical judgment, and that the author's results have been good—about 0.3 per cent. mortality and, as far as he has been able to determine, 4.1 per cent. of recurrences in nearly eleven hundred operations, including those which were done when radical cure procedures were in their infancy—it is doubtful if many modern surgeons will agree with the author as to the advisability of certain practices which he considers indispensable to success. Thus, we believe that few can be found who will pull the omentum out of the abdomen and resect it when it fails to present itself in the hernial sac, or divide the round ligament, or drain the superficial wound. It is likewise doubtful whether many will share his firm and long abiding faith in the power of carbolic acid solution to render the

field of operation "absolutely aseptic," or concur in his opinion that there is great danger of the spermatic cord being injured when it is transplanted according to Bassini's method. These criticisms in no wise detract from the general value of the work. In its entirety we esteem it highly, and can cordially recommend its perusal to all who are interested in the subject of which it treats. C. W. B.

DIE DIREKTE LARYNGOSKOPIE, BRONCHOSKOPIE, UND ŒSOPHAGOSKOPIE. VON DR. MED ET PHIL. W. BRÜNINGS, Privatdozent an der Universität Freiburg I. Br. Pp. 406; 112 illustrations. Wiesbaden: J. F. Bergmann, 1910.

THIS work constitutes an important contribution to the literature of the subject of the direct examination of the upper air passages and the œsophagus. Brünings uses an apparatus of his own device, the light, as in most of the German instruments, being cast from the proximal extremity of the tube through its length. In the United States practically all laryngologists use the Jackson light, which is placed on a carrier and run through the side of the tube, almost directly to the spot which it is desired to illuminate. Aside from this difference, the book in its general description, as regards technique and the various cases in which the method is of value, is in agreement with the views of Jackson and others of the American school. Brüning's illustrations are particularly good. He has some excellent *x*-ray photographs, and other cuts, which are of great value as illustrating the various positions which the tubes assume in bronchoscopy and œsophagoscopy. F. R. P.

THE SEXUAL DISABILITIES OF MAN AND THEIR TREATMENT. BY ARTHUR COOPER, Consulting Surgeon to the Westminster General Dispensary, London. Pp. 184. New York: Paul B. Hoeber, 1909.

IN this small volume Mr. Cooper discusses, in a sane and dignified, although exceedingly brief, manner, the sexual disabilities of man, dividing the discussion into two parts—sterility and impotence. In the first part he treats of the semen, quantitative and qualitative changes in the semen, changes in the zoösperms, and the treatment of sterility; and in the second part, he discusses sexual physiology, primary and secondary impotence, and the local and general treatment of the condition. The booklet is to be recommended to those desiring a brief exposition of the subject, founded upon large personal experience. A. K.

PROGRESS

OF

MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

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The Pupillary Symptoms in Thoracic Aneurysm.—In a clinical lecture OSLER (*Practitioner*, 1910, lxxxiv, 417) showed a patient with a large aneurysm of the arch of the aorta, associated with unequal pupils and absent knee-jerks. In his discussion of the pupillary symptoms of thoracic aneurysm he recognized three groups of cases: In the first of these there is involvement of the sympathetic nerve by direct pressure of the aneurysmal sac. This is, however, rarely met with at postmortem examinations. Clinically, moreover, in most cases of aneurysm, pupillary features are present without other indications of involvement of the sympathetic system—such as unilateral flushing and sweating of the face, ptosis, and retraction of the eyeball. Dilatation of the pupil on one side may, however, be the sole indication of pressure on the sympathetic, and is sometimes met with in pneumonia, apical tuberculosis, and chronic pleurisy. Myosis with profuse sweating and occasional slight ptosis is more common than mydriasis with unilateral flushing, increased heat, and sweating. In the second class of cases the inequality of the pupils depends on the vascular condition of the iris. Wall and Walker believed that the most common cause of anisocoria is unequal blood pressure in the ophthalmic arteries. The vessels of the iris are spiral or zig-zag, and a rise of blood pressure tends to lengthen them and leads to a narrowing of the pupil, while a fall in pressure causes shortening of the vessels and enlargement of the pupil. The variations of pressure in the vessels of the iris do not correspond, however, to the variations in the radials, as the radial pulse may be larger on the side on which

the pupil is smaller. In the third group is found the association of pupillary symptoms, aneurysm, and tabes—the Babinski syndrome—all a part of the syphilitic infection. In these cases the irregularity of the pupils or the myosis is not due to compression by the sac, but is the ocular manifestation of a tabetic or taboparetic state. The Babinski syndrome means merely a condition in which aneurysm is present along with tabetic features—the Argyll-Robertson pupil or unequal pupils, with absent knee-jerks or lightning pains.

The Quantitative Estimation of Albumin in the Urine.—Although the Esbach method is in wide use as the simplest means of quantitative estimation of albumin in the urine, its sources of error and inaccuracies are such as to make it of comparatively little value. In order that any degree of accuracy be obtained the urine must be diluted to a specific gravity of 1006 to 1008, and so that the albumin will read 4 grams or less to the liter, and the temperature should be at or near 15° C. The readings are frequently upset by the fact that the precipitate does not settle, or does not settle evenly, or by the percipitate forming immediately on mixing and thus interfering with the reading of the meniscus. As an improvement on the Esbach method, Tsuchiya has suggested the use of a solution of phosphotungstic acid, as follows: Phosphotungstic acid, 1.59 grams; hydrochloric acid (conct.), 5 c.c.; ethyl alcohol, q. s. ad 100 c.c. This solution is substituted for the picric-citric acid solution and is used in Esbach tubes. MATTICE (*Arch. Int. Med.*, 1910, v, 313) has made a comparative study of the value of this method, and of its modification by Goodman and Stern and the Esbach test, controlling his results by means of the gravimetric and Kjeldahl methods. The method of Goodman and Stern proved to be very inaccurate. Tsuchiya's method, however, gave extremely good results. The precipitate invariably settled more evenly and read closer to the weighings than it did with the Esbach. In a series of cases, readings made at room temperature showed that the average difference in albumin content as compared with the gravimetric and Kjeldahl method was 1.736 with the Esbach and only 0.297 with the Tsuchiya method. The phosphotungstic acid solution is lighter than water, and the urine need not be diluted. The presence of sugar in the urine is of little importance with the phosphotungstic acid. A slight precipitate with readings of 0.5 gram per liter and above in cases of nephritis in which the urine was examined daily showed very close relationship between the Kjeldahl and phosphotungstic acid methods, while the Esbach method proved quite unreliable.

The Relationship Between the Wassermann Reaction and Mercurial Treatment.—KIROLYFI (*Wien. klin. Woch.*, 1910, xxiii, 162) refers to the disappearance of a positive Wassermann reaction frequently noted during vigorous antiluetic treatment with mercury. Since it is not known whether this effect is due to the presence of mercury alone or to its action on one of the bodies concerned in the Wassermann reaction, the author has investigated the action of corrosive sublimate on the test in vitro and in vivo. The test-tube experiments confirmed the facts already noted by Detre and Sellei to the effect that relatively

strong bichloride solutions cause no hemolysis of washed red blood cells, the corpuscles being fixed and sinking to the bottom of the tube. Weaker solutions cause laking of the red cells. The author found that laking occurred with solutions varying in strength between 0.003 to 0.004 per cent. and 0.04 to 0.06 per cent. When bichloride was added to the usual components of the Wassermann reaction, so that its resulting strength would fall within these limits, hemolysis took place, that is, a test which otherwise would have been positive became negative. It seemed probable, therefore, that the disappearance of a positive test during active mercurial therapy was due simply to the mercury in the patient's blood serum. In order to determine this point, luetic patients were studied before and during mercurial treatment. If the negative reaction during treatment is due to the mercury *per se* in the patient's serum, then the inactivated serum should cause hemolysis without the addition of hemolytic serum. As a matter of fact, hemolysis did occur. The interpretation of the result is complicated, however, by the fact that normal human serum contains amboceptors for sheep corpuscles. Therefore, it becomes necessary to remove the complement entirely from the experiment. When this is done, there is no hemolysis, showing that whatever mercury is present is quite inactive so far as hemolysis is concerned. This result indicates, the author believes, that mercury has a specific action on the luetic bodies in the patient's serum.

Experimental Anterior Poliomyelitis.—LEVADITI AND LANDSTEINER (*Compt.-rend. Soc. de biol.*, 1910, lxviii, 417) have continued their studies on poliomyelitis in monkeys by investigating the method of entrance of the virus into the system. The nasal mucous membrane of monkeys in captivity shows an inflammatory process, but this is most marked in infected animals—a fact which points to the possibility of the disease being spread from the nasal passage. To determine whether the nose might be the portal of entrance, a few drops of virus were injected into the nasal mucous membrane of a monkey. Ten days later the animal became paralyzed and died. To find out the path of the infection the two olfactory bulbs of this monkey were triturated with saline solutions and the mixture injected into another monkey. Six days afterward the second animal died. The organism thus probably enters the brain by following the branches of the olfactory nerve. With a view to finding some means of preventing infection by the nasal passages, virulent emulsions of virus were mixed with antiseptics—methylated oil, 1 per cent., and a powder of menthol, salol, and boric acid. Two hours later the mixtures were injected into the spinal cords of monkeys. These monkeys showed only slight, temporary disturbances, while the control animal, injected with the virus alone, became paralyzed on the fourth day and died.

The Results of Cutting the Tawara Bundles.—EPPINGER and ROTHBERGER (*Ztschr. f. klin. Med.*, 1910, lxx, 1) have made a study of the effects of severing the Tawara bundle in the living dog's heart. They find that the cutting of one of the Tawara bundles leads to a visible alteration in the contraction of the heart; the two chambers of the heart no longer beat synchronously, but alternate. Auscultation

frequently gives a well-defined gallop rhythm. The most noticeable alteration is the change in the swing of the galvanometer needle (electrocardiograph). Severing the bundle does not necessarily lead to deleterious effects on the circulation. Provided there has not been much loss of blood, the heart beats with undiminished vigor for some time and the blood pressure is well maintained. The authors were not always successful in cutting the bundle, but in the cases in which the electrocardiogram showed no change, serial sections of the heart proved that the Tawara bundle had not been severed, while the positive cases always showed a lesion of the bundle. The authors have reproduced numerous electrocardiograms, which they discuss at considerable length. They show that the electrocardiogram assumes the form of right-sided extrasystoles when the left Tawara bundle is cut, and vice versa. This is explained by the fact that the right ventricle receives its normal stimulus from the auricle, whereas that to the left ventricle is interrupted by the cut in the Tawara bundle and only reaches it *via* the right ventricle. Furthermore, the result of bilateral cutting of the Tawara bundle brings proof of the physiological fact that the conduction of the simulus to the ventricles is conveyed exclusively by the Tawara bundles. Again, the negative results, where the cut missed the Tawara bundle, show that deep cuts elsewhere in the ventricle do not affect its contraction. The fact that automatism becomes established after cutting the Tawara bundles, just as it does after severing the bundle of His, indicates that the site of automatism may not be situated exclusively in the Tawara nuclei.

Chronic Heart Block in the Dog.—Erlanger and Blackman (*Heart*, 1910, i, 177) report seven instances in which chronic heart block was produced in dogs by injuring the auriculoventricular bundle. Of five of these, all, possibly with one exception, had complete and permanent heart block lasting from six to three hundred and forty-three days. One animal had a relatively complete block from which it recovered in twenty-six days, and one had a slight grade of block which disappeared within forty-eight hours. The average ventricular rate was about 25, while that of the auricles was 129. The ratio of auricular to ventricular rate is thus just about the same as is found in heart block in man. The ventricular rate increased if the animal was nervous, after muscular exercise, but more especially during etherization. Various types of cardiac irregularity were met with. Periodic irregularities, variability of the ventricular rate, and ventricular extrasystoles were rare. More frequent were the periodic irregularities. In association with Cheyne-Stokes respiration, slowing of the ventricular rate occurred more or less synchronously with acceleration of the auricular and respiratory rates. Another type of arrhythmia consisted of periodic, although somewhat irregular, acceleration of the ventricles. The cause of this "group beating" of the ventricles is obscure, but after each series of rapid beats there occurred a stoppage of the ventricles, associated with which there might be vertigo and syncopal attacks similar to those seen in Adams-Stokes disease in man. In comparison to the body weight the heart was hypertrophied to as much as 100 per cent. In one instance the effect of stimulation of the vagus was studied, and it was found that a weak stimulus, but one sufficing

practically to stop the auricles was almost without action on the ventricles, while the strongest stimulation only reduced the rate of the ventricles slightly. Stimulation of the accelerator nerve caused a greater proportional acceleration of the ventricles than of the auricles. In another case the injection of iodine solution into the region of the bundle caused at first a complete block, which later gave way to partial or, at times, a relatively complete block, and finally, after twenty-six days, resulted in a return to a normal conduction. Recovery was apparently due to decompression of the bundle through the removal of the iodine and of the inflammatory exudate. In no case was there any evidence of regeneration on the part of the conducting structures of the auriculoventricular bundle.

The Specific Meiostagmine Reaction.—Ascoli (*Münch. med. Woch.*, 1910, lvii, 62) has discovered a new and, as he believes, specific immunity reaction which he designates the meiostagmine reaction (*μείων*, small, and *στάζω*, to drop). The reaction depends upon alteration of the surface tension of an immune serum plus its specific antigen when tested before and after incubation in the thermostat. The apparatus used is the stalagmometer of Traube, by which the number of drops in a given quantity of fluid may be accurately determined. It was found that corrections for temperature need not be made, provided all determinations are made at room temperature. As a concrete example of the specificity of the meiostagmine reaction, Ascoli presents protocols of experiments performed with sera of typhoid fever patients which agglutinated typhoid bacilli in dilutions varying between 1 to 80 and 1 to 360. The serum was used in a dilution of 1 to 10. As antigen, the author employed the alcoholic extract of typhoid bacilli prepared according to the method of Neisser and Shiga (*Deutsch. med. Woch.*, 1905). The antigen was used in dilutions of 1 to 1000, 1 to 10,000, 1 to 100,000, and 1 to 1,000,000. As a diluent for both serum and antigen, 0.85 per cent. NaCl was used. To 9 c.c. of the diluted serum 1 c.c. of the diluted antigen is added, and the number of drops is immediately determined. The mixture is now placed in the incubator at 37° C. for two hours, removed, and allowed to cool to room temperature. A second determination of the drops is now made. When the antigen was employed in dilutions of 1 to 1000 to 1 to 100,000, the number of drops was always found to be increased by two to three after incubation, this result constituting a positive reaction. Normal sera, used as controls, when united with typhoid antigen, always gave negative results, that is there was no decrease in the size of the drops after remaining in the incubator two hours. Similarly, the substitution of colon bacillus extract as antigen with typhoid serum caused no lowering of the surface tension. The reaction probably depends at least, in part, on substances soluble in alcohol (lipoids), since the alcoholic precipitate, when used as antigen, gave negative results. The reaction shows, the author says, the importance of a more careful study of physicochemical processes in connection with immunity reactions.

The Meiostagmine Reaction in Malignant Tumors.—Ascoli and Izar (*Münch. med. Woch.*, 1910, lvii, 403) report a series of observations

made on the blood of patients suffering with malignant tumors, with a view to determining the possibiility of applying the meiostagmine reaction in such conditions as a means of diagnosis. As controls, they used blood from patients suffering with various other diseases. Preliminary to their observations on human sera, they made a study of normal and sarcomatous rats. The preparation of the sarcomatous antigen is given in detail. Of 9 sarcomatous rats tested, all gave a positive meiostagmine reaction, while 8 normal rats reacted negatively. Using the sarcomatous antigen of the rat, they tested sera from patients and found a negative reaction in 28 cases which were non-malignant (including 2 lipomas), while 29 of 31 malignant tumors, among them 3 sarcomas, gave a positive reaction. (Most of the diagnoses were confirmed microscopically). Since then, the authors have prepared antigen from 6 different human carcinomas and find, to their surprise, that it must be used in very much more dilute solution (1 to 10,000) than was found to be advantageous with the rat antigen. In a footnote the authors state that their material now includes 62 cases of malignant disease, of whom 58 gave a positive meiostagmine reaction. In 48 non-malignant cases a positive reaction has not been encountered. Of the negative (non-malignant) cases, 2 leukemias were included. As yet, they have not had the opportunity of examining the blood of patients suffering with fibromas and myxomas.

A Specific Property of Luetic Sera.—Izar (*Münch. med. Woch.*, 1910, lvii, 182), working in Ascoli's laboratory, has applied the meiostagmin reaction, lately described by the latter, to the study of luetic sera. In all, his observations included twelve different sera, eleven of which yielded a positive Wassermann test. As antigen, the author made use of the alcoholic extract of a spleen obtained from a syphilitic fœtus. The organ was dried and rubbed up; 0.5 gram of the powder was shaken in 50 c.c. of alcohol, placed in the incubator two hours, filtered, and the filtrate condensed to 10 c.c. This stock solution of antigen was then diluted as necessary with 0.85 per cent. NaCl solution. For purposes of control, the luetic sera were united with various other antigens, namely, alcoholic extracts of organs showing tuberculosis, echinococcus, carcinoma, and sarcoma, and watery extract of typhoid. For further control, three sera from patients suffering with leprosy (two of which gave positive Wassermann reactions) were tested with all antigens. Dilutions of the luetic sera varied from 1 to 20 to 1 to 100 in 0.85 per cent. NaCl. For the antigen, the author found a dilution of 1 to 100 in 0.85 per cent. NaCl to be the best. To 9 c.c. of the diluted serum, 1 c.c. of diluted antigen was always added. The author's figures show that in all twelve sera the addition of syphilitic antigen caused an increase of two to five drops, whereas controls never showed an increase of more than one drop, usually only a fraction of a drop. When other antigens were used with the luetic sera, the increase in the number of drops after two hours in the incubator never exceeded one, showing apparently that the reaction is a specific one. The sera from the three patients with leprosy, as well as sera obtained from patients suffering with various other diseases, always reacted negatively. Especially noteworthy was the negative reaction in the case of the two leprosy sera which gave a positive Wassermann reaction.

These sera had been sent to the author simply as sera showing a positive Wassermann test. It was only after the negative meiostagmine test had been obtained that the author learned that the sera were not luetic in origin. Although the results obtained thus far are very encouraging, the author feels that the value of the method as a diagnostic aid is by no means proved with the small material he reports.

SURGERY.

UNDER THE CHARGE OF

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The Indications and Practical Value of Pyelotomy for the Removal of Calculi in the Renal Pelvis, Based Upon a Study of 103 Cases.—PERINEAU (*Ann. d. m. d. org. gén.-urin.*, 1910, 1, 493) considers that pyelotomy is an ideal operation for the radical cure of calculi of the pelvis and calices. It is scarcely more difficult than nephrotomy, which compels the delivery of the kidney. It permits a careful and complete exploration of the pelvis and calices by direct palpation. It avoids damage to the renal parenchyma, since there may be bilateral nephritis, especially marked in old cases. It avoids the possibility of primary or secondary hemorrhage, which has caused death in some cases, and permits catheterism of the ureter to determine its freedom from obstruction, which is essential to an uncomplicated cure. In all cases in which the ureter was clear healing occurred without a fistula. If in uncovering the kidney there is found an accentuated perinephritis preventing or rendering difficult the exposure of the ureter, the operation of pyelotomy should be abandoned. The lacerations and hemorrhage would make the operation a blind one and hazardous. The contra-indication is more marked in pyonephrosis. To expose the calculi and provide for drainage, it is much more rational to make a wide opening in the kidney, which may be the seat of a purulent collection. On the other hand, in cases of slight calculous pyelitis and perinephritis, pyelotomy is not contra-indicated. Then a more careful suture is required, in a double or triple layer. A renal calculus can be removed only by section of the parenchyma where it is enclosed. An attempt should never be made to remove a calculus requiring a large wound of the pelvis, and especially an incision invading the ureter. Every large stone invading the whole renal reservoir, which will be irregular and coral-shaped, ought to be removed by nephrotomy. Multiple, small calculi, according to the experiences of Delbet and Mocquot, should

be removed by a pelvic incision. Practice alone, however, can indicate the best method, and it seems to indicate clearly that nephrotomy is more effective in these cases. In those in which the clinical symptoms point to stone, and palpation of the pelvis does not detect it, Perineau does not counsel an exploratory nephrotomy. The reported cases in which this has been done do not show that nephrotomy has disclosed a stone when palpation has failed. In an anuric patient two accidents may supervene. Uremia may develop even in the beginning, and may compel an immediate and rapid operation. In such a case it is preferable to do a nephrostomy to save the patient's life. If there is a quiescent period, catheterism of the kidney to be operated on should be done. It may remove an obstruction of the ureter or locate the seat of the calculus. The skiagraph may also locate it. If catheterism does not reëstablish the function of the kidney, operation should be done at once and the pelvis exposed. The stone is found here most frequently, and then should be removed by a pyelotomy. The ureter can be probed for a second calculus, which according to Legueu, is nearly always impossible in a nephrotomy.

Treatment of Fractures by Parathyroid Medication.—MOREL (*Archiv. gén. d. chir.*, 1910, vi, 231), as the result of experiments upon animals, believes that the parathyroids play an indisputable role in osteogenesis; that their action is equally distinct in the growth of healthy bone, and the cicatrization of fractured bone; that their action, which is certain on the young organism, seems to be nil upon adults; that all or part of the role in osteogenesis attributed to the thyroid should be assigned to the parathyroids; and that it would be important to make a trial in man of the accelerating action of parathyroid medication in the consolidation of fractures.

Traumatic Lesions of the Semilunar Cartilages of the Knee.—GORSE (*Archiv. gén. d. chir.*, 1910, vi, 244), in accounting for the slight attention given to these injuries in France as compared to England, says that it is partly due to the greater indulgence in sports in England, and to a less systematic examination for the lesion in France, where many of the cases of hydrarthrosis rebellious to treatment, and diagnosticated as tuberculous, are probably due to this cause. He reports a case of subluxation of the external semilunar cartilage with subluxation posteriorly of the tibia. He discusses, however, the more common variety, the dislocation of the semilunar cartilages without concomitant lesions. It is much more frequent in the left than the right knee, and involves the internal cartilage more often than the external. Dambrin, from cadaver studies, determined that the internal cartilage is more poorly fixed, and is thinner than the external, the internal being 3 mm. in thickness, the external 7 mm. Bennett and Jones have classified the possible lesions in essentially the same way. The peripheral attachments of the cartilage may be torn, the anterior and posterior remaining intact. The anterior cornu may be detached, the free end either shrinking up in the interior of the articulation or rolling up on the articulating surface of the femur in the parapatellar groove. The posterior cornu may be detached, but this is so rare as to render it negligible. Transverse fissures of the cartilage may occur, the frag-

ments being drawn inward, and the tibiocartilaginous ligaments and capsule not maintaining the cartilage in place. Longitudinal fissures in the middle two-thirds of the cartilage may take place; the internal fragment, remaining fixed at its two points of attachment, deviates inward. Finally, true luxations may occur, characterized by tearing away of the cartilage either at its periphery or the cornua, with shrinking toward the glenoid surfaces. When the accident occurs there is a sudden fixation of the leg in semiflexion, with a very severe pain and sometimes a distinct crackling sound. Soon there is an intra-articular effusion, usually moderate, and sometimes fugacious. At the inter-articular line, usually antero-internally, there is a prominence or depression, the latter being absolutely pathognomonic. There may be an associated subluxation of the tibia. A systematic examination should be made in each case. The treatment should be carried out as soon as the diagnosis is made, to prevent the development of a chronic joint inflammation. In recent cases reduction of the dislocated cartilage is the first indication. Forced flexion should be followed by sudden extension. A crackling and a return of the joint movements indicate that reduction has taken place. If this fails, it should be done under an anesthetic, and, if necessary, continuous extension should be employed afterward. Three operations have been practised—meniscopexy or fixation of the cartilage by suture, partial and total meniscectomy, or excision of the cartilage. Nearly all authors are partial to excision. Drainage should not be employed if the excision has been easy, but is indispensable if it has been tedious and laborious or whenever there is reason to distrust the asepsis. Dambrin, in 117 cases, did meniscopexy in 36, with 21 perfect results, 10 good results, 3 mediocre, and 1 bad. In 82 cases he did meniscectomy, with 53 perfect results, 26 good, 3 mediocre, and none bad.

The Functional Results Following Resection of the Elbow with the Interposition of Muscle Flaps by Helferich's Method.—REINER (*Deut. Ztsch. f. Chir.*, 1910, civ, 209) says that by the resection of the elbow-joint two objects are sought—to remove the focus of disease, and to give the patient a useful joint. In two years, twenty-eight resections of the elbow joint were performed. The indications were tuberculosis, ankylosis after fractures, irreducible dislocations, polyarthritis, gonorrhœal and suppurative arthritis. Recently the operations have been done almost exclusively under anesthesia induced through the veins. The Langenbeck resection was employed and the incision carried far enough upward to permit a sufficiently large muscle flap to be obtained. The humerus was made convex and the radius and ulna concave, according to Helferich, saving as much bone as possible. A large pedunculated flap was then taken from the radial side of the triceps including a part of the tendon. This was placed in the concave surface of the forearm bones and fixed by a few catgut sutures to the surrounding soft tissues and periosteum, so that a displacement of the flap could not occur, and the bone wounds were entirely covered. The wound was then closed completely by sutures and the arm dressed in complete extension. The dressing was first changed in eight days, and daily after that the joint was alternately placed at an acute and an obtuse angle. Energetic active and passive movements, massage, and hot

air treatment were carried out. In operations for old fractures and dislocations it is very important that all callus, detached fragments of bone and of capsule should be carefully removed, since they tend to produce new bone formation and renewed limitation of motion. The end results were observed in 23 cases; of 2 there was no report and 1 died of unknown cause. In 4 the results were absolutely bad. One of these was a case of recurring myositis ossificans, and should be excluded because the failure was not due to the operation or after treatment, but to the underlying condition. In 21, over 90 per cent. of normal movement was obtained, in 2 under 90 per cent., and in 2 under 30 per cent. Pain persisted in 4, in 19 full function was obtained, in 4 no function, in 1 a marked flail joint, and in 2 complete ankylosis. In 1 of the 4 in which the results were absolutely bad the arm was much atrophied and powerless. The cause was probably in the use of too large an interposed flap and insufficient removal of the disease. In another case the cause of trouble was a high-grade flail joint, and in the third the ankylosis was due to new bone formation. Permission for a second operation was refused. Primary healing is absolutely necessary for the best result, although in a large number good results were observed after healing by granulation, and in three cases even with necrosis of the muscle flap. The numerous modifications and similar operations show the great interest in the method. Interpositions of capsule, tendons, periosteum, fatty tissue, skin, cartilage, and various organic and inorganic foreign substances have been employed, but probably none have given so many and so good results as Helferich's method.

A Contribution to the Surgery of the Liver and Bile Passages.—JENCKEL (*Deut. Ztschr. f. Chir.*, 1910, clv, 1) studied 233 cases involving the biliary passages, of which, 230 were operated on. Of these, there were 7 cases of acute infectious cholecystitis, 100 of chronic recurrent cholecystitis, 22 of hydrops of the gall-bladder, 26 of empyema of the gall-bladder, 24 of calculous obstruction of the common duct, 10 of occlusion of the common duct by tumor, 32 of cancer, and 9 of other diseases of the biliary passages. Of these, 211 were in females and 19 in males. This shows the usual predominance in the female sex, usual at least, in Europe, although among the Japanese, according to Mizokuchi, there were 40 men to 26 women. Of the 230 cases, 30 died, a mortality of 13 per cent.; 9 died from diffuse peritonitis, 6 from pneumonia, 1 from embolus, 4 from cholemia, 3 from cholangitis, liver abscess, and septicopyemia, 3 from heart failure and collapse, 1 from hemorrhage due to erosion of the right epigastric artery from suppuration, and 1 from chloroform anesthesia. The following operations were performed for conditions complicating gallstones: Laparotomy for carcinoma, pancreatitis, etc., in 27 cases; incision for abscess of the abdominal wall in 4; gastro-enterostomy in 6; hepatopexy in 1; liver resection in 3; cecostomy in 1; and entero-anastomosis in 2.

Long-continued Primary Etherization.—MOSKOWICZ (*Zntrlbl. f. Chir.*, 1910, xxxvii, 193) says that Sudeck, Thiersch, and Nettel in isolated cases succeeded in prolonging primary anesthesia with ether combined with morphine injections, for as long as two hours. Moskowicz has

been employing the method for years in an increasing number of cases. It is not unusual to keep up the anesthesia for an hour to an hour and a half, and to perform with it such operations as excisions of the large intestine, of the stomach, and of the ovaries. The patients during the operation respond when aroused, answer to their names, and look around. The condition is not a narcosis, but is best compared to an alcoholic intoxication. Most patients can thus be intoxicated readily with varying quantities of ether, violent men and hysterical women not so easily. A few drops of chloroform may sometimes be necessary. Under its influence the character of the intoxication changes markedly and the patient remains quiet when the ether is renewed.

Methods of Treatment for Air and Fat Emboli.—VON LESSER (*Zntrlbl. f. Chir.*, 1910, xxxvii, 213) calls attention to facts previously published concerning the effect of air in the heart. The heart valves and, especially, the tricuspid are competent in the presence of fluid. If air in large quantity instead of blood fills the heart cavities, the valves become insufficient, and the abnormal contents of the right heart will be pushed backward and forward like a cork between the pulmonary artery and caval veins. If the heart of an animal is exposed through the sternum without opening the pleuræ, and air is introduced into the heart through the jugular vein, the heart will be seen to contract in vain. Gradually, the coronary arteries become filled with air or bloody froth, and soon the contractions of the heart completely disappear. If, now, an indifferent fluid substance (0.5 per cent. saline solution) is injected through the muscle substance directly into the right ventricle, until gradually the fluid becomes greater in quantity than the air, then the heart contents will be gradually pushed onward and the valves again become competent. Soon the blood follows, the heart contractions become stronger, and the circulation is restored. Recent publications have shown that these facts may be employed in the saving of life. Schantz, for example, has recently reported good results in cases of fat emboli, from subcutaneous and intravenous infusions of saline solutions.

Continuous Syphonage of the Stomach in the After-treatment of Severe Cases of Peritonitis.—WESTERMAN (*Zentralbl. f. Chir.*, 1910, xxxvii, 356) says that one of the most important points in the treatment of peritonitis after operation, is to combat the auto-intoxication, which is the result of the interference with intestinal peristalsis. The intestinal contents soon become foul with the production of poisons which are absorbed. Gas formation is marked and irritants are formed which inflame the gastric and intestinal mucosa. In order to avoid this auto-intoxication, the stomach is frequently emptied by an œsophageal tube, but the result is brief and often the introduction of the tube causes great disturbance, so that preference is often given to the formation of an opening in the intestine. But this operation is a severe one in the usually exhausted patient, and unfortunately often does not accomplish the purpose for which it was performed. When it is effective, it is often a life-saving procedure. Usually the opening is made low in the small intestine, in order that the danger of inanition may be lessened and the inflammation of the skin from the irritating

intestinal secretions decreased. On one occasion, Westerman had occasion to make such an opening in the first portion of the jejunum. The patient was almost dead, was vomiting continually a black, stinking substance, and the attempts to empty the stomach by a tube had failed. The formation of the jejunostomy was followed by a cessation of the vomiting, the distended intestines emptied themselves, and the patient recovered. This experience led to the employment, in another case of severe peritonitis, of an œsophageal tube passed through the nose to the stomach and left in position for several days. The result was very encouraging. In twelve hours, 4 liters of intestinal fluid were evacuated from the stomach, and in addition a large quantity of gas. Two days later the stomach contents were only slightly colored with bile and the tube was removed. Since then the stomach tube has been employed in this way in 15 cases with good results. The tube should have a diameter of 0.5 cm., and should not be too thin, since the opening would then close too easily. Two lateral openings should be made in the lower end of the tube, to prevent closure of the tube by the mucous membrane of the stomach.

Volkmann's Deformity of the Ankle as a Result of a Congenitally Faulty Position of the Fibula.—CHRYSOSPATHIES (*Zntrbl. f. Chir.*, 1910, xxxvii, 434) says that all the text books of orthopedic surgery teach that this condition, described first by Volkmann, is a congenital luxation of the foot, due merely to a partial defect of the lower end of the fibula. He has seen two cases within a period of seven months, and is convinced that in his cases, at least, there was not the slightest defect in the fibula. The *x*-rays did not show a defect, and in the second case operation also failed to show it. He found that the deformity was the result of a displacement of the lower end of the fibula, posteriorly and internally. In the first case, a boy, aged four years, the deformity was observed soon after birth, and increased each year, although it did not hinder his running or jumping. The clinical picture was that of the Volkmann deformity, and the foot was in the equinus position with a tense tendo-Achilles. An incision was made behind the internal malleolus at an obtuse angle, the tendo-Achilles was divided at its insertion and sutured to the inner side of the calcaneus in order to place the foot in a varus position, a plaster of Paris bandage fixing it in the over-corrected position. After removal of this bandage the wearing of a supporting apparatus was necessary. The result was not altogether satisfactory. In the second case the external malleolus could be followed in the normal position of the tendo-Achilles. A vertical incision was made over the lower end of the external malleolus. As this was deepened instead of the Achilles tendon the peroneal tendons were found, and deeper the external malleolus. After freeing this bone from the surrounding soft tissues and the tibia, it was found to be of its normal size and form. A place was made for it in its normal position, to which it was forced after breaking the fibula, 1½ fingers' breadth above the epiphysis, the lower fragment then being fixed in its new position with catgut. A plaster-of-Paris cast held it in place and three weeks after operation was removed, when the *x*-rays showed the malleolus in its new position. After the use of an orthopedic supporting apparatus for a short time, the patient could walk normally. Volkmann's de-

formity is shown, therefore, to be due, in some cases, at least, not to a defect in the lower end of the fibula, but to a faulty position of the bone. It is evident that the foot turns inward under the influence of the weight of the body. It is not intended here to deny that the defect which others have reported cannot exist. The purpose is to call attention to the findings in these two cases, and to ask that observations be made to determine which condition is the most frequent.

THERAPEUTICS.

UNDER THE CHARGE OF

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The Treatment of Tuberculosis with Large Doses of Tuberculin.—NEUMANN (*Deutsch. med. Woch.*, 1910, xxxvi, 209) thinks that children can take much higher doses of tuberculin than those ordinarily given. He considers that the local reaction at the site of injection offers the best guide for the treatment. In the event of a local reaction an increased dose must not be given until the reaction has subsided. He reports one case, a rachitic boy, aged four years, who improved markedly under tuberculin treatment. The initial dose in this case was 0.0001 gram. Injections were given at intervals of from one to six days until a dose of 0.5 gram was attained at the end of six months. Neumann advises great caution in using tuberculin treatment when there is any focus near the central nervous system.

The Tuberculin Treatment of Dispensary Patients.—HAWES AND FLOYD (*Boston Med. and Surg. Jour.*, 1910, clxii, 1) draw the following conclusions as a result of their work on this subject: (1) Out of 143 patients with various forms of tuberculosis treated with tuberculin during the past four years, 19 have died, 16 have shown no improvement, while 108 have been benefited to a greater or less degree. (2) In no instance have they been able to see that tuberculin has done the slightest harm; reactions have been rare and invariably of a very mild type. (3) In incipient pulmonary tuberculosis, especially in children, tuberculin is a factor in increasing body resistance and in maintaining this resistance so as to prevent relapses. In more advanced pulmonary disease tuberculin will often alleviate distressing symptoms, prolong life, and occasionally help to arrest the process. (4) In localized or "surgical" tuberculosis tuberculin has a marked beneficial effect. Its administration should always be combined with hygienic outdoor treatment, and in the vast majority of instances should be subservient to this. (5) Dispensary patients can be treated with tuberculin not only with perfect safety, but with benefit, providing there is a close personal coöperation between patients and physician.

The Results of the Combined Sanatorium and Tuberculin Treatment of Pulmonary Tuberculosis.—BANDELIER (*Beiträge z. klin. d. Tuberkulose*, 1910 xv, 1 to 180) gives a very exhausive report of the combined tuberculin and sanatorium treatment of 500 cases of pulmonary tuberculosis. Only 18 of the 500 cases (13.8 per cent.) were not benefited and these were all in the third stage of the disease. In 17.2 per cent. of the total number the patients were apparently cured. He divides the cases that improved into two general classes—those who regained full earning capacity and those who regained sufficient earning capacity for the legal standard. The cases that regained full earning capacity comprised 90.4 per cent. of 83 first-stage cases, 80.7 per cent. of 286 second stage cases, and 32.8 per cent. of 131 cases of the third stage. The cases that attained the legal standard in their earning capacity were divided into 9.6 per cent. of the first stage cases, 19.3 per cent. of the second stage cases and 53.4 per cent. of the third stage cases. Thus, he denotes his results as positive in 100 per cent. of first and second stage cases and in 86.2 per cent. of third stage cases. The most striking results were shown in the 286 cases of the second stage. Bandelier believes that the conflicting results obtained by different observers with the tuberculin treatment may be explained by variations in the length of the tuberculin treatment. He thinks that such a treatment, to be effective, must be carried on for a considerable period of time. Bandelier's average period of treatment was from five to six months. He advises giving the tuberculin until the maximum dose is reached, and then injecting this maximum dose at constantly increasing intervals. He gives many details of the treatment and instructive tables.

Intravenous and Intramuscular Injections of Large Doses of Antitoxin in the Treatment of Diphtheria.—BERLIN (*Deutsch. med. Woch.*, 1910, xxxvi, 210) writes of his experience with the intravenous and intramuscular injections of antitoxin in 120 cases of diphtheria. He found that from 4000 to 16,000 units had a much quicker curative effect than smaller doses. In 34 cases the temperature became normal on the day following the injection, and in 28 cases this happened on the second day. Coincidently with the fall in temperature the pulse rate fell and there was a marked improvement in the general condition. The improvement in the local inflammation in the throat was not so marked. Berlin prefers the intravenous method, and injects the serum into one of the arm veins. In the case of children intramuscular injections into the gluteal muscles are preferable. Berlin believes this method is harmless, and advocates it especially when quick results are desired.

Autoserotherapy of Ascites.—AUDIBERT and MOUGES (*Presse médicale*, 1910, xviii, 81) report their results in a case of ascites due to liver disease treated by subcutaneous injections of the patient's own ascitic fluid. Their technique is similar to that of Gilbert in tuberculous pleurisy. They aspirate the fluid by means of an aspirating syringe and divert the needle into the subcutaneous tissue when withdrawing the needle from the peritoneal cavity. In the case reported they commenced with an injection of 3 c.c., and gradually increased this dose to 10 c.c. The injections were made at intervals of six days, and twelve

injections were given. The procedure was painless and there was no local or general reaction resulting from the injection. They claim that the injections caused an abundant and persistent diuresis, which was the main factor in producing the subsidence of the ascites. Coincidently with the diminution in the ascites there was a marked improvement in the general condition. Audibert and Mouges withdrew salt from the diet, and consider this withdrawal an important part of the treatment. However, they apparently do not consider that the withdrawal of salt might explain in great measure the diuresis.

The Treatment of Carcinoma with Body Fluids of a Recovered Case.—HODENPYL (*Med. Record*, 1910, lxxvii, 359) describes a case of carcinoma of the breast that apparently terminated in a spontaneous cure. Four years ago the patient underwent a radical operation. The morphology of the tumor was typical of a rapidly growing carcinoma. Multiple recurrences appeared in the neck and in the scar resulting from the operation. These were removed, but further recurrences developed in the neck and breast which were not removed owing to the general condition of the patient and certain local complications. Later, large tumors developed in the liver, so that the liver nearly filled the abdominal cavity. This was followed by an excessive chyliform ascites. The prognosis was considered hopeless. However, the tumors in the neck and breast gradually disappeared. The abdominal tumors gradually diminished in size until the liver became approximately normal in size and position. The chyliform ascites which necessitates frequent tapping is the only marked remaining indication of the previous trouble. Hodenpyl, on the theory that there was some curative substance in the ascitic fluid, tested the effects of injections of the ascitic fluid into mice that had developed tumors as a result of inoculation with some of the well-known strains of mouse cancer cells. He injected the ascitic fluid into the tumors, adjacent to the tumors, or into tissues remote from the tumors. The effect of these injections was a marked necrosis of the tumors leading to a considerable diminution in their size and often to their complete disappearance. The harmlessness of the ascitic fluid was first determined by injections into animals and into human beings, and then Hodenpyl tried its effects in cases of carcinoma of various types in man. Small injections were made near or directly into the tumors, or large amounts of the fluid were injected intravenously. A temporary redness, swelling, and tenderness occurred about the tumors. This soon subsided and was followed by a softening and necrosis of the tumor tissue which was either absorbed or discharged externally. The tumors have grown smaller in all cases, and in some cases have entirely disappeared. The injections have had no effect upon other tissue than tumor tissue, and there has been no systemic effect even after large intravenous injections.

The Management of Glycosuria in Elderly Persons.—VAUGHAN (*New York Med. Jour.*, 1910, xci, 417) says that the glycosuria of elderly patients is very often dietetic and is frequently due to the excessive ingestion of some particular forms of carbohydrate. The particular forms of carbohydrate that are not tolerated should be detected and

excluded from the diet. Furthermore, the limit of tolerance for other carbohydrates should be determined and these carbohydrates given to the point of tolerance. Vaughan states that the capacity for assimilating carbohydrates depends largely upon the time of day they are ingested. Thus glycosurics who excrete sugar upon carbohydrates taken at breakfast may dispose of 100 grams of carbohydrates taken at a six o'clock dinner. Finally, Vaughan lays stress upon the value of the open-air treatment of this form of glycosuria. He thinks that sleeping in the open air is as beneficial to the glycosuric patient as to the tuberculous patient.

Acidosis in Diabetes and the Value of the Oatmeal Cure.—Tüthje (*Therapie d. Gegenwart*, 1910, li, 8) writes that in general the daily amount of acetone bodies excreted in the urine gives a measure of the severity of the disease. He believes, however, that the administration of alkalies can markedly increase the excretion of the acetone bodies without any increase in the formation of these bodies, and consequently without any added danger to the patient. Furthermore, he believes that the harmful effects of the acetone bodies is dependent upon the duration of the acidosis. Thus, an acidosis of a mild degree, but long continued, is more to be feared than a higher acidosis of short duration. The acidosis that persists when a patient remains sugar-free on a strict meat and fat diet is harmless according to Tüthje. Therefore, he believes it is not necessary to change the strict diet so long as the patient remains sugar-free. However, if such a patient excretes sugar, a daily quantitative estimation of the acidosis is necessary for a rational treatment. Tüthje speaks of the good effects of the oatmeal diet in severe cases of diabetes with acidosis, and advances an hypothesis for its action. He suggests that the oatmeal starch may exercise a true exciting action upon the fermentative processes which possibly play a part in the metabolism of glucose in the body.

The Determination of Acidosis in Diabetes from a Therapeutic Standpoint.—Blum (*Therapie der Gegenwart*, 1910, li, 97) calls attention to the articles of Tüthje and of Gulmuyden, who claim that a quantitative estimation of the acetone bodies is necessary for a rational treatment of severe cases of diabetes. Blum agrees with their findings that such a quantitative estimation is ideal, but points out the practical difficulties of such an estimation. He suggests the determination of the ammonia nitrogen as a measure of the severity of the acidosis. Such a determination is simple and is an accurate measure of the grade of acidosis when no alkali is being taken by the patient. Blum believes that the amount of alkali necessary to render the urine alkaline is a measure of the severity of the acidosis, and he advocates this method of determining the severity of the acidosis. Normally from 5 to 10 grams of sodium bicarbonate are sufficient to make the urine alkaline. Mild cases of acidosis require 20 grams of sodium bicarbonate, moderately severe cases require 20 to 30 grams, and severe cases require 50 grams and over. It is often impossible to render the urine alkaline, especially in cases of acidosis that have advanced as far as coma. Blum believes that the carbohydrates should never be entirely withdrawn until the urine has been rendered alkaline.

The Dietetic Treatment of Uric Acid Diathesis and Gout.—Bessau and Schmid (*Therap. Monatsh.*, 1910, xxiv, 116) discuss briefly the part played in gout and the uric acid diathesis by the exogenous uric acid. They include in their article valuable tables of the purin content of various foods. They found that there was no appreciable difference in the purin content of red and white meat and but little difference in the meat of different species of animals. In general the purin content was greater in the smaller species of animals. Fish contained approximately a higher purin content than meat. The purin content of such small fish as sardines, anchovies, and sprats was very high. Consequently they consider that they, with liver, kidneys, and thymus, belong to the purin-rich foods. They also found that spinach, peas, beans, and lentils contained a high percentage of purin bases. Some varieties of mushrooms were also found to be rich in purin bases. Bessau and Schmid state that the part played in uric acid metabolism by purin bases derived from vegetables is not definitely known, but that they are not to be disregarded as a possible source of exogenous uric acid.

Glycerin in the Treatment of Pernicious Anemia.—Vetlesen (*Semaine Méd.*, 1910, xxx, 45) has used glycerin with success in the treatment of two cases of pernicious anemia. He bases this treatment on the theory that pernicious anemia is due to the hemolytic action of a lipoid substance similar to oleic acid. Glycerin forms an inert ether (triolein) when combined with oleic acid, according to Vetlesen. Therefore he gave the glycerin, hoping for a similar combination with the lipoid substance, which is, according to this theory, the cause of pernicious anemia. Half an ounce of glycerin with the juice of half a lemon is given three times a day. In one case treated by this method the blood showed a hemoglobin percentage of 20 and a red cell count of 900,000, with corresponding changes in the morphology of the red blood cells. After seven weeks treatment the hemoglobin content increased to 90 per cent. and the number of red cells to 4,700,000. The patient also gained about thirty pounds in weight.

Veronal in Delirium Tremens.—Möller (*Berl. klin. Woch.*, 1909, xlvi, 2340) reports good results with the use of veronal in delirium tremens. His routine method of treatment is as follows: On admission into the hospital, one gram of veronal was given, and if no sleep followed within three hours, a second dose of one gram was given. This second dose was seldom required. A third dose may be given within five to six hours in very severe cases. Sleep usually came on rapidly and lasted from six to twelve hours. The patient usually was clear and quiet upon awakening. A half gram of veronal was sufficient to control any tremor if present. If insomina persisted, a half gram of veronal given at night was ordered. Of over 100 cases treated, this treatment only failed in 3. Of this series only 2 died, 1 as a result of a double pneumonia, the other from general weakness due to repeated attacks of delirium tremens. Möller says that this method of treating delirium tremens has the great advantage that it is eminently suitable for home treatment.

PEDIATRICS.

UNDER THE CHARGE OF

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The Bacteriology of Acute Infections of the Respiratory Tract in Children.—L. EMMETT HOLT (*Archiv. Int. Med.*, 1910, v, 449), on account of the increase of acute respiratory diseases among children, especially in institutions, has made a study to determine how much of the trouble was due to influenza. Nothing was accepted as of diagnostic value except the presence of Pfeiffer's bacillus. Cultures were taken from all cases of catarrhal inflammation of the upper and lower respiratory tract, and also from cases of pneumonia, empyema, otitis, and all febrile cases of doubtful diagnosis. Blood-agar plates were used for all cultures. Observations were made on 250 children and cultures obtained from the blood of 59 consecutive autopsies. The Bacillus influenzæ was discovered by culture in 85 cases. Of 47 cases of acute bronchitis and pneumonia during winter and spring, the bacillus of influenza was found in 63 per cent. During the warm months this bacillus disappeared and was found only once. Pneumococcic infection, however, persisted during the hot weather. Cultures made after paracentesis in 29 cases of acute otitis showed the staphylococcus 25 times, the pneumococcus nine times, and the bacillus of influenza not a single time; and yet 15 of these 29 cases gave positive throat cultures for Bacillus influenzæ. Cultures were made from the lungs and heart's blood in 59 consecutive autopsies. Of the 47 made in winter and spring, 17 showed the bacillus of Pfeiffer. In the 12 autopsies made in summer the bacillus was not found. Of 58 persons suspected of having influenza, the throat cultures were positive in 42 and negative in 16 cases. The proportion of positive throat cultures in suspected cases, 73 per cent., is large enough to warrant it an important result. Bacillus influenzæ is pathogenic and plays a more important part at certain seasons of the year. It is often associated with the pneumococcus, modifying the clinical course of a pneumonia. 16 healthy persons showed Bacillus influenzæ repeatedly, often in pure culture. These become real sources of danger as carriers. Acute otitis is to be regarded as a complication of influenza. Acute nephritis may occur as a complication. Recurrent attacks of influenza are probably relapses and not fresh infections from without. No single clinical type is diagnostic of influenza. The lower respiratory tract is the favorite seat of the bacillus and it may persist there for weeks.

Constipation in Infants.—ERIC PRITCHARD (*Practitioner*, 1910, lxxxiv, 583) states that constipation is nearly always due to mechanical interference at the colon and sigmoid, or to dislocation of the sensitive reflex of the rectum. In cases of nervous debility with loss of tone of the muscles, the intestinal musculature is also involved. Constipation is one of the most frequent complications of rickets, and there is a tendency to it in meningitis and in cretins and mentally defective

infants. Irregular habits are usually formed during the first few weeks of a baby's life, purgative drugs being especially harmful. The nerve centres in the cord tend to fall into periodic habits from recurring stimuli. Severe attacks of diarrhœa predispose to subsequent constipation. A deficient quantity of food is a common cause in breast-fed infants. Constipation from overfeeding is more common in bottle-fed infants. The particular element of food responsible is still in doubt or dispute. The following conditions may cause constipation: Congenital malformations; acquired structural alteration; interference with the nervous mechanism of peristalsis and defecation; faults in the intestinal contents; insufficiency and deficiency of fluid. Prophylaxis is the best form of treatment A test feed should be taken, weighing the baby before and after a feeding to determine the quantity it is getting. Periodicity of evacuations should be encouraged. Do not under- or overfeed, nor use aperients and purgatives. Pritchard offers as a good lubricant, pure liquid petroleum, 20 minims to the dram in emulsion. He also suggests aromatic elixir of cascara and tincture of nux vomica in emulsion of petroleum.

The Condition of the Blood in Pertussis.—Hugh T. Ashby (*Brit. Med. Jour.*, 1910, i, 1105) has made a study of the blood of nearly 100 children suffering from pertussis. A differential count was made in every case. The age of the children was from nine months to nine years. The blood was taken at various stages of the disease, and specimens from the same case were repeatedly examined. In a fair proportion of cases the number of leukocytes was increased from 15,000, to 30,000. The hemoglobin and the number of red corpuscles showed no important variations. Leukocytosis is a valuable aid in the diagnosis of suspicious cases. Only in rare instances did the leukocytes reach this number in bronchitis and afebrile chest conditions. In those cases with a well-defined whoop the lymphocytes formed about 60 per cent. of the white cells. The preponderance of the lymphocytes, especially the small variety, is noticeable. After the whooping stage is passed the lymphocytes diminish, and reach the normal number in about two months. The total number of polymorphonuclear cells is but slightly increased. If the lymphocytes form nearly 60 per cent. of the number of white cells it is confirmatory evidence of pertussis. In septic conditions the polymorphonuclear cells are increased in number.

OBSTETRICS.

UNDER THE CHARGE OF

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Pubiotomy a Justifiable Operation.—Williams (*Amer. Jour. Obst.*, May, 1910) publishes the results of 25 pubiotomies, with no maternal and three fœtal deaths, one of which could be attributed to the opera-

tion. These patients were delivered by forceps or version immediately after the operation. The bladder was uninjured and there were six perineal and five deep communicating vaginal tears in the series. Twelve of the cases were primiparæ. The absence of severe injury was attributed to restricting the operation to moderate grades of pelvic contraction, the use of Döderlein's method, and extensive manual dilatation of the vagina and perineum before operation. In delivering the child, to avoid injury it is best to make horizontal instead of upward traction. In the after treatment, a four-inch strip of adhesive plaster was sufficient to hold the pelvis. Patients usually moved in bed between two and four days, were out of bed by the twentieth, and were discharged on the thirtieth day with satisfactory locomotion. Healing occurred by fibrous union, leaving well-defined mobility between the ends of the bone in two-thirds of the cases. Williams estimates that maternal mortality should not exceed 2 per cent. with competent operators and in uninfected unexhausted patients. The operation is indicated in contracted pelves with a true conjugate above 7 cm., and in funnel-shaped pelves after a test of several hours in the second stage of labor has shown the necessity for operation. In breech extractions, and in transverse presentations treated by version, it may be best to place the saw in position before delivery, so that the pelvis can be opened as soon as it can be seen that the child cannot pass without difficulty. In multiparæ with repeated difficult labors, or in primiparæ with excessive disproportion, pubiotomy is inferior to Cesarean section at the end of pregnancy or the beginning of labor. Williams takes the view that the test of labor renders Cesarean section dangerous, but does not prevent the successful performance of pubiotomy in cases of moderate pelvic contraction. He believes that in uninfected women pubiotomy should replace high forceps, prophylactic version, induction of labor, and craniotomy upon the living child. It is not to be employed upon infected patients or after other means to deliver have failed. It must be considered as a primary operation the dangers of which are infection, hemorrhage, and deep lacerations. When, during the operation, the ends of the bone do not separate wider than 4 or 5 cm., patients recover well and are able to walk and work as well as ever. Permanent enlargement of the pelvis in the transverse diameter of the outlet, and, to a slight degree, in the true conjugate, follows the operation when the pelvis heals with fibrous union. This enlargement, in a subsequent pregnancy, may be sufficient to permit spontaneous labor. If not, the operation may be repeated, while Cesarean section should be limited to cases in which the pelvic contraction is marked and the child is large.

Five Cases of Hebotomy.—HOLLÄNDER (*L'Obstétrique*, April, 1910) reports five cases of hebotomy after Döderlein's method in which the mothers recovered. There were no wounds of the bladder nor serious hemorrhage. The puerperal period showed fever in one case. In one patient elevation of temperature after delivery was found to be due to tuberculosis. In one patient the child presented by the breech and was born asphyxiated, and could not be revived. In this case delivery by section would undoubtedly have saved the life of the infant. In one patient there was flat and generally rachitic pelvis with a true

conjugate of 8 cm. After the pelvis had been opened there was very little rotation of the two halves, and it was found that at the left sacro-iliac articulation there was cicatricial tissue which prevented rotation at the joint. This cicatricial tissue made a practical ankylosis. In this patient, after pubiotomy, the child could not be delivered by forceps, and craniotomy was necessary.

The Duration of the Second Stage of Labor and its Influence on Mother and Child.—KÖNIGSBERGER (*Zntrbl. f. Gyn.*, No. 18, 1910) has observed 5000 cases in which labor was unduly prolonged in the second stage. In the more severe of these cases the patient's life was endangered through laceration of the soft parts, fever, septic infection, and rupture or atony of the uterus; while the child was brought in danger through asphyxia. It was observed that when the second stage of labor lasted more than eight hours the mortality for mothers reached 15 per cent. The percentage of fatal asphyxia among the children rose from 1 per cent., its normal average, to 10 per cent., when the second stage of labor lasted more than eight hours.

A Case of Precipitate Labor Causing the Death of the Infant.—HAUER (*Zntrlbl. f. Gynäkologie*, No. 18, 1910) reports the case of a patient in her second pregnancy, who was suddenly delivered while standing. The whole duration of labor was but fifteen minutes. The child fell upon the floor, the umbilical cord ruptured, and the mother fainted. The child weighed 3480 grams, and died from hemorrhage from the torn umbilical cord. The mother recovered. The case is interesting from a medicolegal standpoint, as illustrating the death of the child without the connivance or action of the mother. Hemorrhage from the torn umbilical cord rarely becomes serious, and had the mother remained conscious, suspicion might naturally have been aroused regarding her possible action in the matter.

The Treatment of Placenta Prævia in the Munich Clinic.—MAISON (*Zntrlbl. f. Gynäk.*, No. 18, 1910) reports 154 cases of placenta prævia treated by the use of the tampon, elastic bags, ruptured membranes, or version. The entire mortality of the mothers was 14 per cent. In central placenta prævia the mortality rose to 28 per cent., while the death rate for the children was 75.8 per cent. If only those cases are reckoned in which the child was in fair condition upon admission, the mortality is reduced to 68.7 per cent. The highest mortality rate for the mothers followed the use of the tampon in treatment, and reached 25 per cent.; of the children, 70 per cent. Maternal deaths occurred in these cases partly from bleeding and partly from septic infection. The worst results were seen in Polyclinic cases treated by the tampon. The cases treated by the Braxton-Hicks method were divided into two groups, in one of which extraction immediately followed version; while in the other extraction was delayed. In 31 cases treated by version without extraction, the maternal mortality was 10 per cent.; the fœtal mortality 80 per cent. The mortality of the children when extraction immediately followed version was 60 per cent., without maternal mortality.

Congenital Dislocation of the Kidney into the Pelvis Complicating Pregnancy.—HALBEIN (*Wien. med. Woch.*, No. 4, 1910) reports the case of a multipara who had a tumor in the small pelvis. It was found that this was in such a position that labor could not occur, and accordingly abdominal section was performed. The tumor was found to be a good sized healthy kidney. It was carried upward under the sigmoid flexure to the capsule of the kidney and sutured to the peritoneum. The patient suffered from abortion. Experience shows that 80 per cent. of these cases are upon the left side, and that they are sufficiently frequent to occasion confusion in diagnosis. Malformation of the genital tract is often present, and operation is frequently necessary for successful delivery. The kidney should not be removed unless it is found essentially diseased, but whenever possible operation should not be undertaken until the patient has recovered from pregnancy and labor. If the kidney is diseased it should be removed. Should it be necessary to perform Cesarean section, the kidney should be fixed in its normal position at the conclusion of the operation.

Villous Toxemia and the Serum Diagnosis of Early Pregnancy.—FIEUX and MAURIAC (*Ann. de gyn. et d'obst.*, February, 1910) believe that in early pregnancy there is intoxication from the villi of the chorion, which makes the serum diagnosis of pregnancy a possibility. This seems probable, because some of the diseases of pregnancy occur early and cease immediately when the ovum dies. Should the ovum persist, these disorders gradually cease about the third or fourth month, when the syncytium is less active. Should an extensive degeneration of the chorion occur, as in hydatid degeneration, the patient may become worse. Eclampsia usually develops comparatively late in pregnancy when the syncytium is not abundant, while the villi of the chorion are best developed in early pregnancy. A villous toxemia theoretically should be found early in pregnancy. The writers endeavor to demonstrate this by making an antigen, the portions of the placenta being removed from the sixth to the tenth week of pregnancy. In 55 observations 5 were negative in pregnancy lasting from three to five weeks; 8 were positive in pregnancy lasting from two to three months; and in pregnancy from three to four months, 1 was positive, 4 negative, and 2 doubtful; in 14 cases from the fourth to the ninth month of pregnancy all gave negative results. Negative results were also obtained in 10 patients in whom pregnancy could not be diagnosticated by its clinical signs. In 3 abortions, from the second to the third month of gestation, results were positive; while in 7 cases from the fourth and fifth months of pregnancy, the results were all negative. These observations led to the conclusion that in some periods of gestation the blood of pregnant patients contains a substance which in the presence of young villi disturbs the equilibrium of metabolism. The antibody in the blood appears when the chorion is most active. Its function is to neutralize poisons formed in the placenta and check the activity of the trophoblasts. Patients were examined who had fibroid tumors and who had syphilis but were not pregnant, and in these the reaction was not obtained. These observations recall those of Grafenberg, who isolated a ferment from the chorion between the second and fourth months of pregnancy. This presumably acts upon the internal tissues, permitting their penetration by villi.

GYNECOLOGY.

UNDER THE CHARGE OF
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The Spread of Carcinoma by the Fallopian Tube.—GLENDINING (*Jour. Obst. and Gyn., Brit. Emp.*, 1910, xvii, 24) records a preliminary note on two cases of secondary carcinoma disseminated by the Fallopian tube occurring in association with secondary growth in the ovary. In each instance the primary growth was in the stomach. In both instances there were found in the Fallopian tube, and permeating its tissues, numerous minute and discrete cancerous deposits arranged in such a manner that it is not at once easy to determine in what direction they are passing, or at what point or points they have entered the tissues. He believes the microscopic study of these tissues, together with some other points brought out, prove that cancer cells floating in the peritoneal cavity are swept into the lumen of the Fallopian tube, and there coming in contact with the lining, pass through the columnar epithelium to enter the lymphatic spaces of the subepithelial and muscular tissues, and so pass into the mesosalpinx. This method, Glendining believes, has never been mentioned in literature.

Primary Cancer of the Fallopian Tube.—Primary cancer of the Fallopian tube is made the principal feature of the January, 1910, number of the *Jour. Obst. and Gyn., Brit. Emp.* Besides the article of DORAN and GLENDINING abstracted and appearing herein are clinical reports of three cases by Herbert Spencer, one by Tate, and one by Legg. A careful microscopic study is reported by each recorder.

Changes in the Normal Endometrium During Menstrual Life.—NORRIS and KEENE (*Surg., Gyn., and Obst.*, 1910, x, 44) have carefully studied the changes in the normal endometrium during menstrual life. One hundred cases constituted the material studied. It is concluded that the endometrium in the normally menstruating woman undergoes a complete and definite cycle every twenty-eight days. For the purpose of study, this cycle is best divided into four periods which blend into each other. During the period which constitutes the premenstrual process the endometrium takes on all of the changes common to the decidua vera at a very early stage, only at this time the changes are of a lesser degree. As soon as free hemorrhage occurs, the congestion is relieved. The postmenstrual and interval periods constitute a process of repair. Each of these periods possesses definite histological characteristics, the most typical changes being found in the premenstrual and postmenstrual periods. As has been said, the periods blend into each other and are subject to slight variations in different individuals. The menstrual period lasts from four to six days, the postmenstrual three to five days, the interval from ten to twelve days,

and the premenstrual about ten days. It is therefore important that the pathologist, when examining endometrium, should know when the last menstrual period occurred. This knowledge, combined with an understanding of the changes during the various transformations of the normal endometrium, will show that many of the cases diagnosticated as glandular or interstitial endometritis are nothing more than different periods of the normal endometrium, and, consequently, that endometritis, in the true sense of the term, is much less frequent than is commonly thought. In the classification of endometritis, they recommend its division into acute and chronic, doing away with the cumbersome and faulty classifications which are now used.

The Subinvoluted Uterus.—R. R. SMITH (*Surg., Gyn., and Obst.*, 1910, x, 17) reports his study of the changes in the uterus occurring in subinvolution of that organ. This study is extended into the treatment of that condition, which included various plastic operations, the employment of drugs, and waiting for the menopause to produce atrophy. Smith believes there is a class of cases that cannot be successfully treated by such measures; in fact, only removal of the body of or the whole of the uterus will suffice, and records 23 cases thus treated successfully. In 9 the blood loss at or between menstrual periods was very serious. In 9 there was great pelvic discomfort. Retroversion and prolapse were present in 7. The principal reasons for hysterectomy were long continuance of the symptoms, severe loss of blood, the non-relief by simple procedures, the age of the patient, and the size and condition of the uterus.

Tetanus Developing Twelve Days after Shortening the Round Ligaments.—R. PETERSON (*Jour. Amer. Med. Assoc.*, 1910, liv, 108) reports a case of tetanus developing twelve days after an operation for shortening the round ligaments, and his conclusions are based upon this case and 150 others following surgical operations found in literature. From these Peterson concludes: (1) While tetanus cannot be said to be a very frequent postoperative complication, a study of the reported cases shows it does occasionally follow all kinds of gynecological operations. (2) It most frequently is a complication of operations involving the opening of the peritoneal cavity, although in quite a percentage of cases it complicates plastic and other non-peritoneal operations. (3) The infection in all probabilities is introduced at the time of operation. (4) It has been proved that the tetanus bacillus and its spores are most difficult to kill, and that under certain circumstances they survive boiling for sixty minutes; hence when this organism is present more than ordinary heat, applied over a longer time, is necessary. (5) Absorbable ligatures, like catgut, may be carriers of the infection, unless the most approved methods of sterilization be employed. (6) The process of manufacture of the catgut renders it peculiarly liable to infection by the tetanus bacillus, which may not be destroyed by the ordinary methods of chemical sterilization. (7) The initial symptoms of postoperative tetanus appear within ten days in from two-thirds to four-fifths of the cases. The onset of symptoms in the remaining cases varies from the eleventh to the twenty-second day after the operation. (8) In the 150 cases tabulated no case showed symptoms of tetanus the first two days after

the operation. (9) From a study of these cases it would seem that the average period of incubation for postoperative tetanus was about eight days. (10) The shorter the incubation period the more virulent and active the disease, and, conversely, the longer the incubation the milder the disease or the longer is it possible for the patient to survive before a fatal issue. (11) Whenever possible the point of entrance of the tetanus bacilli should be ascertained and the proper disinfection and drainage instituted. This is often difficult in cases of postoperative tetanus. (12) Antitetanic serum acts on the free toxins in the blood, but has no effect on the toxins after they have become fixed in the nerve cells. (13) A study of the tables shows that the motrality of tetanus has been reduced nearly 10 per cent. through the use of antitetanic serum. (14) The best effects of the serum will be seen when its administration is begun on the first appearance of the symptoms of the disease. (15) Chloretone is able to control the muscular spasms of tetanus and to do away with the muscular rigidity. It is harmless and does not prevent elimination. (16) In tetanus, elimination through free catharsis and the administration of salt solution is of the utmost importance.

Is the Routine Exhibition of the Pre-operative Purge Defensible?—EDWIN WALKER (*Amer. Jour. Obst.*, 1910, lxi, 63) discusses the subject of the routine employment of purgatives in the preparation of patients for operation, and concludes the practice is pernicious. Of it Walker says purgatives can do harm and should be given only when indications are clear. The profession should abandon the slipshod, routine methods now in vogue and should teach the laity, both by precept and example, the evils of the purgative habit. The practice of purging all patients before surgical operations is unnecessary and injurious; they are made more uncomfortable, are weakened, and the condition of the intestinal canal is not rendered more favorable, but, on the contrary, germ activity is stimulated just as it is in enteritis, increasing the probability of infection when the gut is opened, and there is in addition to this more postoperative tympany. A diet of digestible food for twenty-four hours or more and a fast of eight or twelve hours before, puts the intestine in the best possible condition for any operation, especially on the intestinal canal, except where obstructive lesions exist, and for these purgatives are worse than useless, and other measures are required. In a few cases of milder fecal stasis a purgative several days before operation, followed by enemas are of service; these are, however, extremely rare. The routine use of any powerful drug is to be deplored, and the habitual pre-operative purge is indefensible.

Pelvic Transplantation Metastasis as a Means of Recognition of Hopeless Abdominal Carcinoma.—DUDLEY W. PALMER (*Surg., Gyn.*, and *Obst.*, 1910, x, 154) has studied pelvic transplantation metastasis of abdominal carcinoma and has found it is so very common that he has reached conclusions as follows: (1) Rectal examination is absolutely necessary in all abdominal tumors. (2) Of 435 consecutive cases of carcinoma of the upper abdomen 6.5 per cent. showed pelvic transplantation deposits as the earliest clinical sign of inoperability. 7.2 per cent, of stomach carcinomas had this sign. (3) 55 per cent. more cases

were shown to be inoperable, through a thorough rectal examination for pelvic metastasis, than because of the presence of supraclavicular gland metastasis. (4) Pelvic metastasis warrants a most unfavorable prognosis as regards life expectancy.

DISEASES OF THE LARYNX AND CONTIGUOUS STRUCTURES.

UNDER THE CHARGE OF

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Tuberculosis of the Trachea and Thyroid Gland.—GUTHRIE (*Jour. Laryng.*, May, 1910) reports a case of tuberculous disease of the trachea leading to cartilage necrosis and involvement of the thyroid gland. A man, aged forty years, with pulmonary tuberculosis, left a sanatorium within two months after entrance without further physical signs of disease, and with entire absence of bacilli. There was slight respiratory stridor, apparently due to a mass in the anterior portion of the trachea about an inch below the glottis. Tracheotomy was performed under local anesthesia, and on exposure of the isthmus of the thyroid gland it was found infiltrated with newgrowth. Division of the isthmus revealed erosion of portions of the first and second tracheal rings at this point, whence an opening led through a mass of growth into the lumen of the upper end of the trachea. Masses removed from both these situations showed marked tuberculous changes. A few days later the tuberculous masses were removed after splitting the larynx, all surfaces were scraped and rubbed with pure lactic acid, and the lumen was then packed with iodoform gauze down to the level of the tracheotomy tube. The patient did well, and when last seen, some six months before this report, there was no evidence of the return of the tracheal disease.

Sarcoma of the Nose.—PRICE BROWN (*Canadian Jour. Med. and Surg.*, January, 1910) reports a number of cases in which he had successfully relieved the patient of sarcoma of the nose by treatment with the electrocautery. Of seven cases, three had permanently recovered, there having been no return after intervals of fourteen, seven, and two and three-quarter years. The fourth died from toxemic poisoning. The fifth had no return in seven months, and the sixth and seventh had no return in the last two months.

Iodine in Diseases of the Mouth.—TALBOT (*Jour. Amer. Med. Assoc.*, April 2, 1910) lauds the topical application of tincture of iodine in diseases of the mouth. He specially recommends a solution containing zinc iodide, 15 parts; water, 10 parts; iodine, 25 parts; and

glycerin, 50 parts, to be painted monthly, during the school term, over the gums and mucous membrane of public school children to prevent infection and to retard the decay of the teeth.

Palatopharyngeal Adhesions the Result of Traumatism in Operation Upon the Tonsils.—In discussing palatopharyngeal adhesions and the methods adopted for their relief, ROE (*Jour. Amer. Med. Assoc.*, January 15, 1910) describes a new operation which he devised for the relief of a case of practically complete occlusion in a woman, aged twenty-four years, whose condition was the result of traumatism which had been produced in attempting to excise the tonsils one year previously. Practically, the operation consists in separating the parts and covering the raw surfaces with plastic flaps taken from the sound sides of the palate and passed from before backward. For details the reader must be referred to the original.

Tuberculosis of the Œsophagus.—GUISEZ (*Archives internat. de laryngologie, d'otologie, et de rhinologie*, March and April, 1910) reports several cases of tuberculosis of the œsophagus. He distinguishes three forms: (1) Superficial ulceration at the uppermost portion of the œsophagus, announced by painful dysphagia, and attended with spasm or contracture just above the lesion. (2) And more frequently tuberculosis by propagation, with symptoms of œsophageal compression, the walls having to be pushed aside by the œsophagoscope during inspection. (3) The sclerotic type, described by Schrötter, and certainly the rarest. In this the dysphagia is not painful. There is a concentric thickening of sclerocicatricial consistence, as determined by pressure with a probe.

Papilloma of the Larynx and Palate in the Same Subject.—WYLIE (*Jour. Laryng.*, April, 1910) reports the case of a cabdriver, aged forty years, with hoarseness of eight months' duration, and attacks of dyspnœa latterly on lying down. A large subglottic papilloma was seen in the anterior commissure of the larynx, and there were two papillomatous growths on the edge of the soft palate at equal distances from the uvula.

Singers' Node.—PORTER (*Jour. Laryng.*, April, 1910) reports a case of singers' node removed with forceps. Perfect functioning resulted. A microphotograph of the section shows several layers of epithelium on the surface, with vascular connective tissue below, in one part of which the nuclear stain had taken somewhat faintly.

Traumatic Injury of the Upper Air Passages from Formaldehyde.—ELY (*Jour. Amer. Med. Assoc.*, April 2, 1910) reports a case of a boy, aged three years, who attempted to drink a few drops of a 40 per cent. solution of formaldehyde. Postmortem examination, six hours after death, showed a marked thickening of the mucous and submucous coats of the epiglottis, larynx, and trachea, with a superficial necrosis which extended to the bifurcation of the latter. There were no pathological changes discovered in the œsophagus, nor any other evidence of destruction of the mouth and pharynx.

PATHOLOGY AND BACTERIOLOGY.

UNDER THE CHARGE OF

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The Etiology and Pathological Anatomy of Rheumatic Myocarditis.—E. BRACHT and WÄCHTER (*Deut. Archiv f. klin. Med.*, 1909, xcvi, Heft 5 and 6) quote Ashoff and Tawara as describing certain nodule in the heart which were specifically characteristic of rheumatic myocarditis. The specificity of these nodules they say has been disputed by some observers, but all observers have found them. Not all rheumatic cases show the nodules, but where present it is always in rheumatic hearts. The nodules described by the present authors were found in three out of four cases whose clinical diagnosis had been rheumatism. In two of the three cases streptococcus was found in the blood. The authors describe perivascular subendocardial nodules or scars containing large cells and giant cells, and surrounded by a zone of lymphoid elements with occasional leukocytes and plasma cells. Often a proliferation of fibroblastic cells was seen. The adjacent muscle bundles often suffer from pressure, so that when the number is great, distinct effect on the function of the heart muscle results. There seemed to be a tendency for the nodules to occur in the neighborhood of the auriculo-ventricular bundle, with a directly damaging result to that structure. But there are often found in old hearts whose function is undisturbed, many of these rheumatic scars, so that their disposition is apparently more important than their number. Efforts to find a cause for the nodules in the action of bacteria in and about the scars were fruitless. Bracht and Wächter then inoculated animals with Diplostreptococcus rheumaticus. Subsequently the heart muscle was found sprinkled with areas of necrosis in which could be seen proliferation of fibroblast cells, going on to the large cell and giant cell formation described above, with an encircling zone of lymphoid cell infiltration and a few plasma cells. Myocarditis produced by other strains of streptococci showed the usual reaction of tissue to bacteria, that is, gathering of polymorphonuclear leukocytes and often abscess formation.

Experiments upon Increased Blood Pressure in Nephritis.—ALWENS (*Deut. Arch f. klin. Med.*, 1909, xcviii, 137) has modified some methods used by Schlayer to study the effect upon the blood pressure of decreasing the calibre of the renal vessels. It has been long known that one or both renal arteries may be tied off without an accompanying rise in blood pressure, but Katzenstein found in certain experiments that occlusion of the small vessels of the kidney by thrombus masses was followed by an elevation of blood pressure. By means of oncometers

Alwens has compressed the kidneys using a pressure varying from 90 to 135 mm. of Hg. Compression of the entire kidney by this means produces a rise in the systemic pressure of from 20 to 26 mm. of Hg. This phenomenon seems to be absolutely dependent upon compression of the small vessels of the kidney for ligation of the renal artery prevented any rise. He also shows that simple compression of a kidney which is deprived of its blood supply will not influence blood pressure. The reason for this rise of pressure is not perfectly clear. It is apparently not associated with a nervous reflex acting upon the other vessels of the body, for the rise in blood pressure still took place after freeing the kidney pedicle from nerves, section of the splanchnic nerve, and section of the medulla. Neither is it due to a sudden increase in the amount of blood in the body for direct infusion of much larger quantities of fluid is incapable of increasing blood pressure. In spite of the fact that the action seemed independent of the nervous system, still it was thought possible that contraction of the vessels of other organs might account for the rise of pressure. When the left kidney was compressed, however and the right kidney put in an oncometer no change in the size of the kidney was observed. Comparison of the other internal organs gave somewhat similar results. With compression of the spleen the rise in pressure was quite marked, but not constant; with the coils of intestine the rise was still less marked and very inconstant. Compression of the limbs, on the other hand, never gave rise to increased pressure. Alwens believes that compression of the small vessels of the extremities is compensated for by dilatation of the vessels of the internal organs, whereas there is no such mechanism to compensate for the compression of the well protected abdominal organs. The difference in the quantitative changes in the pressure in these experiments and in the contracted kidney in man are so great that it is almost impossible to apply the purely mechanical theory of heightened blood pressure in nephritis upon these grounds.

The Present Status of Trachoma Bodies.—In 1907 Halberstädter and Prowazek described certain bodies which they had found in the epithelial cells of trachoma granules, but which could not be found in the normal conjunctiva or in diseases of the eye other than trachoma. These bodies could be transferred from man to monkey and from animal to animal though every inoculation was not successful. Later Graefe, Frosh, and Clausen stated that they could be found not only in the epithelial cells of the conjunctiva of early cases of trachoma, but in old cases as well and in the eye secretions and cells of the follicles. LINDNER (*Wien. klin. Woch.*, 1909, xxii, 1742), who has studied the question for some time, has confirmed these observations and gives a detailed description of the bodies which he considers to be the cause of the disease. Recently Heymann reported that he had been able to demonstrate bodies in the epithelial cells from cases of conjunctivitis neonatorum which could not be distinguished from those described by Prowazek. To control this discovery Lindner examined 31 cases of conjunctivitis neonatorum. In this category are placed all cases of purulent conjunctivitis of the new born, but 3 cases, which were old must be excluded since the findings were negative. Of the other 28, 13 were due to the gonococcus and though the organisms were occasionally seen within epithelial cells, forming masses which might be mistaken for trachoma

bodies, neither in 12 of these cases nor in 8 cases of gonorrhœal conjunctivitis of adults could true trachoma bodies be found. In one of the cases of gonorrhœal conjunctivitis of the new born, however and in all the other 15 cases of blennorrhœa neonatorum typical trachoma bodies were found. Lindner considers this of great significance and believes that this conjunctivitis of the new born and trachoma are one and the same disease caused by the same parasite. This view was strengthened by the fact that an ape inoculated with material from a case of conjunctivitis neonatorum in which the peculiar bodies were present developed after a preliminary conjunctivitis typical trachoma granules in which were found the trachoma bodies. He believes that infection of the eye takes place during birth and from the vagina, which may be the seat of the disease.

Calcium and Cardiac Inhibition.—It has been shown by Schiff that a solution of physiological sodium chloride allowed to perfuse the heart of a living frog until all the blood is washed away causes immediate cessation of the cardio-inhibitory action of the vagus nerve. BUSQUET and PACHON (*Jour. de. phys. et de path. gen.*, 1909, xi, 807, 851) have repeated and confirmed these experiments in an isolated frog's heart. Many different salts of sodium were employed but they all had the same effect. When minute traces of calcium were added to the saline solution the cardio-inhibitory action of the vagus was immediately restored and with the removal of the calcium salts was equally rapidly lost. Further experiments showed moreover that calcium was absolutely necessary for the preservation of the cardio-inhibitory action of the vagus. The salts of the nearly allied metals such as K, Sr, Ba, and Mg were all infective. Calcium, however in various forms could be employed with success. It was even active in such organic substances as gum arabic and gelatin. When the salts of Na were injected intramuscularly or subcutaneously the cardio-inhibitory action of the vagus was disturbed only by a small group including the carbonate, oxalate and citrate. These salts, as could be shown later, are capable of making Ca inactive and their action seems to be much the same as in the prevention of coagulation of the blood by decalcification. If in the closed circulation an isotonic solution of NaCl be substituted for the blood the cardio-inhibitory action of the vagus is still well preserved even after twenty hours. This is probably due to the fact that small traces of calcium are constantly being washed from the organs of the body into the blood whence they are carried to the heart.

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